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ANTEPARTUM ROENTGENOGRAPHIC DIAGNOSIS OF FETUS PAPYRACEOUS[1]

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FETUS papyraceous is easily diagnosable by antepartum roentgenograms at any time between the death of the twin fetus and delivery. The death of one fetus usually occurs between the third and fifth month of pregnancy. A careful search of the literature, however, reveals but one case correctly diagnosed roentgenographically before delivery (19). Kerr and Rypins (10) demonstrated the fetus papyraceous roentgenographically antepartum, but it was incorrectly interpreted until after delivery. We are reporting herewith a second case so diagnosed, and four other cases of fetus papyraceous in which the opportunity to make the diagnosis roentgenographically was not offered.

Fetus papyraceous (or compressus) is the dead, mummified, and flattened fetus associated with a living twin. Mosher (13) made a complete survey of the literature in 1917 and found only 88 cases reported up to that time. Twenty-six of the reported cases were from America.

Since 1917, we have found 16 additional cases in the literature which, with the five herewith reported, brings the total to 109. Four of the recent reports concern cases of triplets with fetus papyracii (3, 5, 14, 21), and one of them (Beierlein, 3) collected 20 cases of triplet pregnancy with twin fetus papyracii and added one of his own. Beierlein stated that the diagnosis could but rarely be made antepartum and expressed a doubt that the fetus papyraceous would be demonstrable roentgenographically. The incidence of fetus papyraceous, according to Petzold (16), from the Frauenklinic in Vienna, is six times as common in single ovum twins, with double amnii and a single chorion as in double ovum twins. It more frequently occurs in primipara.

The history may give a clinical suggestion of what has happened. In many of the reported cases, there is a history of bloody discharge or actual bleeding at the time of fetal death, which usually occurs between the fourteenth and twentieth week of pregnancy. A bloody discharge is common to so many conditions during pregnancy that one would not suspect the death of a twin fetus unless the second sign were also present. This is the presence of an enlarged uterus, larger by palpation and measurements than one would expect from the duration of normal single pregnancy. The third clinical hint as to what is going on is the regression of the larger-

[1] Presented in part before the New England Roentgen Ray Society, Feb. 18, 1938.

than-normal uterus to normal size after the bleeding occurs, with subsequent normal development, as would be expected in the usual single pregnancy. The diagnosis of fetus papyraceous has been reported to have been made several times before delivery by vaginal palpation of the small fetal structures protruding ahead of the presenting part of the living fetus. The most accurate method, however, is the demonstration of the small but well ossified skeleton of the fetus papyraceous in the roentgenogram (Fig. 1).

The cause of death of one of the twins may not be evident, but it is assumed that the fetal circulation is shut off. This is based on the finding of an infarcted atrophic or fibrosed placenta belonging to the dead fetus. When the blood supply is shut off and the fetus dies, the liquor amnii is resorbed and the dead fetus becomes compressed between the amniotic sac of the living twin and the uterine wall. The removal of the liquor amnii with its enzymes, which play an important rôle in the production of maceration, allows the fetus in its dry aseptic state to mummify. Complete dissolution of the dead fetus is possible only in the early weeks of pregnancy and cannot occur after it has reached any considerable proportions (Williams, 23). The usual sequence of events in single pregnancy with death of the fetus is maceration and abortion. Only in multiple pregnancy does the mummification occur which results in fetus papyraceous. Occasionally an extra-uterine fetus may die and become calcified—fetus, placenta and all—and thus form a lithopedion, which is also demonstrable roentgenographically, but that is a different process. It is extremely rare to find a lithopedion in the human uterus, but it is more common in the lower animals (Williams, *loc. cit.*).

It is important to recognize this complication as delivery may be delayed or hindered by the fetus papyraceous. In two of our cases, labor was delayed by the dead fetus presenting with the presenting part of the live twin. In the other three there was no complication; in fact, in one case (Case 2) the obstetrician did not realize that the placental structures contained a fetus papyraceous. In some of the reported cases a false diagnosis of the presentation was due to the fetus papyraceous presenting before the living twin. The third and most important complication which may arise is the retention of the fetus and its membranes after delivery of the normal twin. The atrophic and fibrosed placenta in several instances was quite firmly adherent to the uterine wall and was separated from it with difficulty. Retention of these non-viable tissues favors, of course, postpartum sepsis.

The roentgenograms have been useful in determining the age of the fetus papyraceous. The fetus does not lose any appreciable amount of its calcium content, and since it usually attains a fetal age of three to five months before death, the ossification centers are well developed. The usual body measurements, except for the foot length, are unreliable, as the fetus is flattened and compressed. We have, therefore, depended upon the appearance of certain centers of ossification, as described by Hess (8), for determination of fetal age, in addition to the usual body measurements.

The other case diagnosed antepartum by roentgenograms was reported by Schinz (19). A translation of his report is roughly as follows:

"As a curiosity I will describe an observation of my own in regard to twins. In this case one of the twins was undeveloped as a fetus papyraceous, whereas the other twin was a fully developed child (Fig. 2237). The diagnosis was correctly made before delivery.

"The diagnosis was made possible by a number of centers of ossification which were lying in one line below the head of the normally developed fetus visible at the entrance of the pelvis. The diagnosis was confirmed at delivery. The presenting fetus papyraceous had to be delivered first, following which the second fetus was born spontaneously."[2]

[2] This case was also reported and the illustration copied by P. H. Schumacher in *Ergebnisse der Medizinischen Strahlenforschung*, **VI**, 294, 1933, in his article on "Die Roentgendiagnostik in der Gebürtshilfe." We are indebted to Dr. Isaac Gerber for calling our attention to this reference.

Our five cases, in brief, are as follows:

Case 1. Mrs. J. A. C., 29 years old, primipara, wife of a physician. Family history and past history unessential. Catamenia began at 16 years, never regular, only two or three times a year, lasting one week. Last menstrual period was Nov. 21, 1936 (date of first visit to obstetrician, Feb. 1, 1937). Physical examination was negative. The duration of pregnancy was estimated at two and one-half months, but the patient was definitely certain that pregnancy did not take place until after Christmas. The menstrual periods had been so irregular that dates based upon cessation of menses could not be relied upon. The size of the uterus seemed much bigger than it should be, dating from a pregnancy after Christmas. Successive examinations on Feb. 19, March 12, and April 1 all indicated a larger uterus than normally expected in a pregnancy of the stated duration. From April 22, on to the termination of labor on Sept. 25, the uterus was not abnormally large. There was no history of injury or illness to account for the death of one fetus. There had been no bleeding or bloody discharge during this period. The Wassermann test was negative.

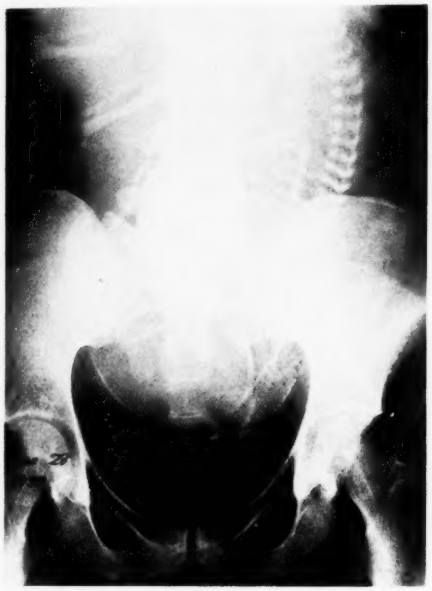

Fig. 1. Case 1. Antepartum roentgenogram three months before delivery, showing well ossified fetus papyraceous on left side of pelvis below and lateral to the head of the viable normal fetus.

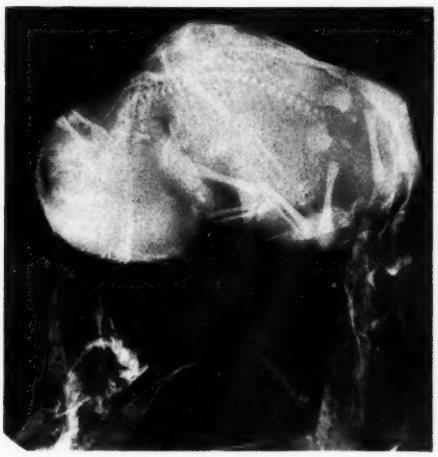

Fig. 2. Case 1. Roentgenogram of fetus papyraceous after delivery, showing the degree of ossification of the fetal skeleton. Estimated bone age, 16.5 weeks.

Roentgenograms were taken on June 28, 1937, by Dr. Richard Dresser at the Collis P. Huntington Memorial Hospital (Fig. 1). These demonstrated a well developed fetus in cephalic presentation and a small fetal skeleton lying on the left side of the pelvis below and lateral to the normal fetal head.

The normal baby, a girl, was delivered Sept. 25, 1937, by Dr. R. S. Titus, by a simple forceps with the head in sight, after a short labor. The fetus papyraceous was delivered with the placenta and membranes, without difficulty. There was no bleeding after delivery.

The pathologic report, by Dr. Fred Ripley, Boston Lying-in Hospital (S-37-909), described the fetus papyraceous and the completely infarcted placenta with two amnii and one chorion. The two placentæ

were fused for a distance of 13 cm., but the infarcted fibrosed placenta of the fetus papyraceous was only 4 cm. wide at its widest point and only 4 mm. in thickness. It had been implanted low, either marginal or a partial placenta previa, a possible cause of the fetal death. The umbilical cord was 12.5 cm. in length. The fetus measured 14.5 cm. in (crown-rump) length, indicating an age of 18 weeks. The pregnancy was interpreted as single ovum twins.

Fig. 3. Case 2. Roentgenogram of fetus papyraceous after delivery. Skeleton well ossified but somewhat macerated. Estimated bone age, 21 weeks.

Roentgen examination of the fetus (Fig. 2) showed well defined centers of ossification for the ilium and ischium, but none for the pubic bone. A study of the other centers of ossification and comparison with the tables reported by Hess (8) gave a bone age of from 16 to 17 weeks.

Case 2 (S-35-34). E. O., aged 38, Para V, was delivered Jan. 12, 1935, of a normal male baby and a macerated male fetus papyraceous. Delivery was uncomplicated. The fetus is the largest in this group, with a C. R. length of 190 mm. and a foot length of 40 mm., with a resultant estimated age of 22 weeks. Dr. Hertig interpreted the placentæ and membranes as a double ovum twin pregnancy.

The roentgenogram (Fig. 3) shows the skeleton well developed with some collapse of the cranial bones. The age by development of the ossification centers is between 21 and 24 weeks, probably nearer 21 weeks as the center for the sternum is not present.

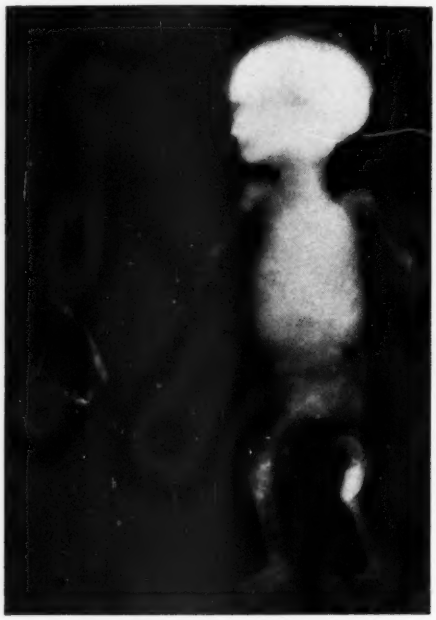

Fig. 4. Case 3. Roentgenogram of fetus papyraceous after delivery. Fetal skeleton poorly ossified, probably a case of osteogenesis imperfecta. Impossible to identify many centers of ossification. Bone age not determinable from roentgenogram.

Case 3 (S-35-204). Mrs. B., aged 23, went through a normal pregnancy, with no bleeding and no excess size of the uterus noted. She was delivered March 10, 1935, by Dr. Benjamin Tenney, with simple low forceps. The living twin was a full term male and the fetus also was male. It measured 110 mm. in C. R. length, 17.5 mm. foot length, which gave an estimated fetal age of fifteen and one-half weeks. There were two placentæ, the one

attached to the fetus papyraceous being shrunken, fibrosed, and immature.

The roentgenogram (Fig. 4) of the fetus shows ill defined bones of amorphous structure with multiple fractures and abnormal ossification. This is presumably a case of osteogenesis imperfecta, in biovular twins. The bone age by roentgenograms was not determinable due to the poor detail and amorphous structure of the bones.

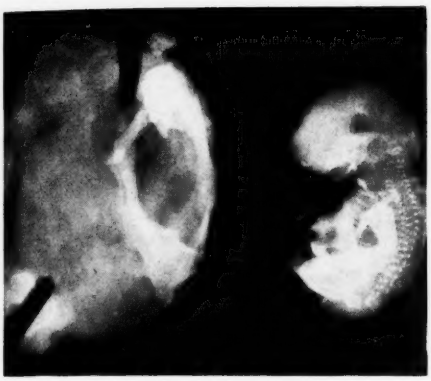

Fig. 5. Case 4. Roentgenogram of fetus papyraceous after delivery. Smallest and youngest fetus in this series, but skeleton is quite definite. Estimated bone age, 11 weeks.

Case 4 (S-36-734). M. R., aged 44, wife of a WPA worker, was a pre-eclamptic, Grade 1, with moderate hypertension, in her tenth pregnancy. There was no history of injury or illness to account for the death of one twin. She was delivered at the Boston Lying-in Hospital on July 29, 1936, of a normal male baby by breech extraction, followed by the fetus papyraceous and placenta. The C. R. length of the fetus was 70 mm. (possibly inaccurate due to distortion). The foot length was 14 mm., estimated age 13 weeks. Dr. Hertig interpreted the pregnancy as biovular twins. The sex of the fetus compressus was not definite.

The roentgenogram (Fig. 5) of the fetus shows it to be the least developed of the five. The ossification centers indicate an age of only 11 weeks.

Case 5 (S-37-843). This patient, R. R., was delivered at the Boston Lying-in Hospital shortly before Case 1 was admitted. The patient, a primipara, aged 35, pre-eclamptic, Grade 1, was delivered Sept. 10, 1937. Her last menstrual period was Dec. 8, 1936. Her past history revealed toxemia and mild hypertension, B. P. 170/98. Hinton and Wassermann tests were negative. She was delivered by low forceps after median episiotomy due to dystocia incident to secondary uterine inertia. The presence of the fetus papyraceous was not discovered until the secundines were examined in the department of pathology. The obstetrician noted a foul odor and "old calcified blood clot" when the placenta and membranes were delivered. The normal living twin was a female. The fetus (male) and placentæ weighed 620 grams. The umbilical cord of the compressed fetus was 53 cm. in length, and was looped once around the neck and twice around one arm. There were separate and intact membranes (amnion and chorion) around the fetus. The C. R. length of the fetus was 10.5 cm., sug-

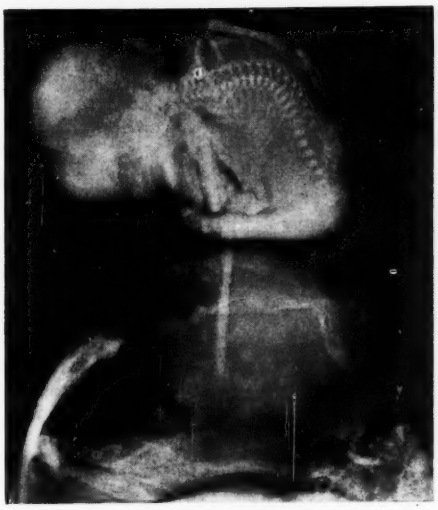

Fig. 6. Case 5. Roentgenogram of fetus papyraceous after delivery. Ossification centers indicate a fetal age of 14 weeks.

gesting a fetal age of 15 weeks. The placenta of the fetus papyraceous was light yellow in color, firm, obviously infarcted and fibrosed. Figure 6 shows the roentgenogram of this fetus. The age by ossification centers was 14 weeks. The pregnancy was double ovum twins.

CONCLUSIONS

1. Fetus papyraceous is probably more frequent than the literature would indicate.

2. The diagnosis can reliably be made by antepartum roentgenograms.

3. The age of the fetus can be determined by the centers of ossification and it may be more reliable than the conventional measurements due to shrinkage or elongation by compression.

4. A case of fetus papyraceous, successfully diagnosed by roentgenograms three months before delivery, is reported, and the roentgenograms of four other fetus papyracii are included to demonstrate the ossification of the fetal skeleton in similar cases.

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THE ROENTGENOLOGIC ASPECTS OF BRONCHOMYCOSIS[1]

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ACCURATE roentgenologic diagnosis of pulmonary infiltrative lesions is notoriously difficult in many of the patients seen in our everyday work. In some of these cases we must resort to laboratory examination of the sputum in order to establish the diagnosis. This is especially true of the bronchomycoses in which the roentgen manifestations are so protean as to defy exact classification in most instances.

Pulmonary tuberculosis is the disease most often confused with the mycoses and many cases of bronchomycosis have been discovered in tuberculosis sanatoria after having been there for varying periods of time. Norris (7) reports the discovery of yeasts in the sputum of 15 per cent of the cases in a tuberculosis sanatorium. While undoubtedly these did not all represent cases of bronchomycosis *per se*, yet as secondary invaders they are of considerable importance in cases of chronic lung infections. Many cases of bronchomycosis are clinically and pathologically similar to tuberculosis and the two can be differentiated only by prolonged sputum examinations. It should be emphasized that the presence of fungi in the sputum does not in itself justify the diagnosis of a primary fungus infection but it should indicate further studies to determine what rôle they play in the patient's problem.

The incidence may show a geographical distribution. Coccidioidal granuloma was first described in California and it is largely confined to that portion of the country. Blastomycosis is more common in the central and southern States, and all mycoses are more frequently seen in the tropics.

A simple classification of the bronchomycoses is given by Castellani (3), as follows: 1. Due to yeast-like fungi, *viz.*, fungi of the types *Monilia*, *Cryptococcus*, *Saccharomyces*, *Blastomycoides*, and *Endomyces*. 2. Due to filamentous fungi: (*a*) of the slender type, *viz.*, fungi of the types *Nocardia*, *Anæromyces*, and *Vibriothrix;* (*b*) of the larger type, *viz.*, fungi of the types *Oidium* and *Hemispora;* (*c*) with characteristic fructifications—*Aspergillus*, *Penicillium*, *Mucor*, *Rhizomucor*, *Acremoniella*, *Sporotrichum*, *Acladium*, etc.

It is impossible in this communication to attempt the description of the changes produced by all of these organisms but a brief discussion of some of those more commonly encountered will be given.

Blastomycosis.—This is a highly fatal, uncommon disease which is caused by infection by blastomycetes—a variety of yeast-like fungi. Some believe that other organisms may be concerned in the etiology, but in many cases the organisms in pure culture have been obtained and the disease reproduced in animals.

The most characteristic lesion is a chronic skin lesion with abscess formation, ulceration, and thickening of the epidermis. These abscesses may involve the subcutaneous tissues, lymph nodes, viscera, bones, etc. Rupture of the abscesses, with discharging fistulæ, frequently takes place.

The pulmonary lesions are less common than those mentioned above, but a number of cases with postmortem examinations have been reported, so that the pathologic changes have been well established. Stober (11), after studying a number of these cases by postmortem examination, states that acute laryngitis and bronchitis are usually associated with active pulmonary lesions and pleural in-

[1] Presented before the Twenty-fifth Annual Meeting of the Radiological Society of North America, at Atlanta, Dec. 11–15, 1939.

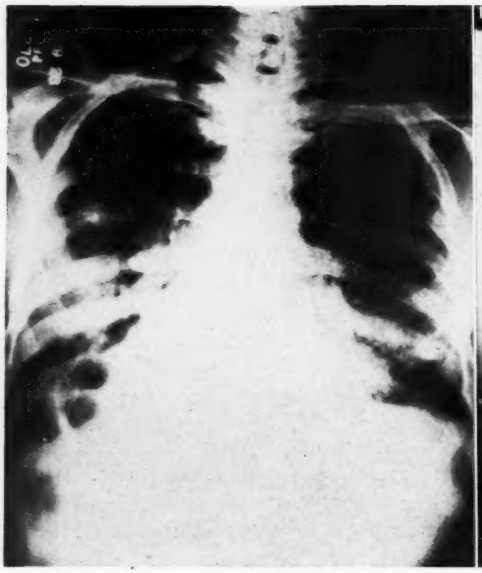

Fig. 1, Case 1.

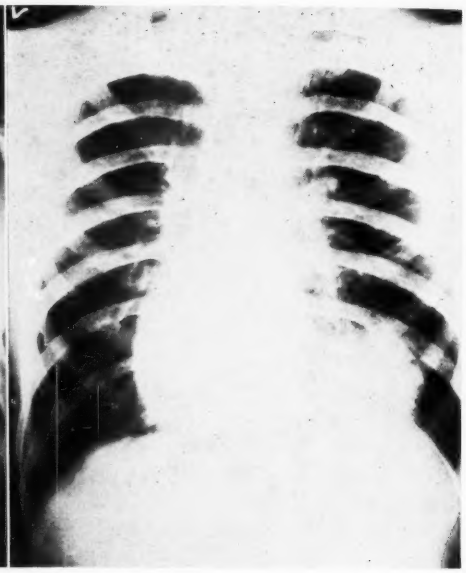

Fig. 2, Case 2.

volvement. The active pulmonary lesions showed a great deal of fibrous tissue around areas of infected lung tissue, frequently in the upper lobes. A number of cases showed evidence of diffuse hematogenous infection.

The clinical picture often simulates that of tuberculous infection and, indeed, the pathologic picture at autopsy may at first be thought to be that of tuberculosis. To make a positive diagnosis, the presence of blastomycetes must be demonstrated in the lesions themselves, although if they are present in the sputum of a case in which the presence of tuberculosis can be excluded the diagnosis is highly probable.

The pathologic changes disclosed on the roentgenogram often simulate those seen in cases of tuberculosis. There may be considerable increase in the hilar areas and in the bronchovascular markings, with an unusual studding following these markings. Brooksher (1) quotes Dunham regarding a characteristic studding which follows one or more of the main trunks, but which does not quite reach the periphery. There is usually an area of lung density around the periphery.

In the same case there may be patches of bronchopneumonia. Some of the changes may suggest miliary tuberculosis but there is usually more fibrosis present in bronchomycosis. Pleural reaction is common in these cases. Cavities filled with necrotic material are of frequent occurrence.

Case 1. White male, aged 60. The patient was admitted to the hospital complaining of "lumps all over the body." For three months previous to the admission he had been expectorating a considerable amount of thick sputum, which was sometimes tinged with blood. A slight cough was also present. Three weeks previously a small lump appeared on the forehead; this was not tender or painful. Since then similar lesions had appeared all over the body, even in the roof of the mouth. These lesions were small, elevated, ulcerating areas with necrotic centers, from which oozed a seropurulent discharge. There was generalized lymphadenopathy.

Examination of the chest disclosed limited respiratory movement. There was impairment on percussion over both sides of the chest, and coarse moist râles over both upper lobes.

The roentgen films of the chest showed extensive parenchymatous infiltration throughout both lungs. The infiltration was of the miliary type with areas of coalescence in the bases, producing partial consolidation in those areas (Fig. 1).

A direct smear from a lesion on the left forearm showed typical blastomycetes. Biopsy of one of the lesions resulted in the finding of blastomycetes, which are seen as heavy rings with clear inner zones, usually lying in areas surrounded by round, wandering cells and polymorphonuclear leukocytes.

The patient declined rapidly and died on the sixth day after admission.

Postmortem examination: The significant findings were as follows: Widely scattered over the skin were fungoid lesions ranging from 1 to 4 mm. in diameter, and elevated above the skin as much as 1 cm. in places. The papillomatous mass was easily scraped away and consisted of a soft granular scab covering a slightly depressed shallow ulcer covered by thin, yellow, purulent material.

The lung margins were firm and rounded, similar to liver tissue. On sectioning the lungs, the smaller bronchioles were filled with purulent material. The pulmonary parenchyma was firm and densely infiltrated with small, gray, pin-point nodules which were quite firm in consistency. There were no areas of cavitation.

Similar areas of miliary infiltration were found in the spleen and kidneys. There were abscesses in the prostate gland and in both sternoclavicular joints.

Examination of material from all these areas showed evidence of cutaneous and systemic blastomycosis.

Actinomycosis.—This is an uncommon but not rare disease, caused by organisms with branching mycelia which often break into segments. The organism which is most commonly present is the bovine type or "ray fungus" and is recognized by the so-called sulphur granules found in pus. This disease is somewhat more common in those living in rural communities, and especially in those persons caring for cattle. It is not known, however, that the disease is acquired directly from cattle but probably comes from fungi which live on vegetation.

About 15 per cent of all the cases of actinomycosis observed clinically are found to involve the thorax. The infection may involve both the chest wall and lungs. Good (6) states that actinomycosis of the thorax falls into four groups: (1) broncho-actinomycosis; (2) pneumo-actinomycosis; (3) pleuropneumo-actinomycosis, and (4) thoracopulmonary actinomycosis, or those cases in which the thoracic wall is involved as well as the lungs.

Pulmonary infection is often secondary to infection in other parts of the body. Aspiration is another source of infection. This has been demonstrated by the finding of aspirated material in the lungs surrounded by the organism. The pulmonary pathology has been described by Christison and Warwick (4), according to the type of lesion present in the lungs. In the bronchitic type, pus and fungi are found; this type is rare. In the pneumonic type, the alveoli are filled with pus and it resembles a bronchopneumonia. These areas may coalesce and form abscesses. In the third type the abscesses may burrow through and involve the pleura where pus accumulates. It may then pass into the fourth type, in which the chest wall is involved. The lower lobes are usually involved first.

The symptoms are similar to those of other pulmonary infections, and include chills and fever of an irregular type, night sweats, loss of weight, pain, and abundant sputum which may contain pus or blood. The diagnosis is usually made by the finding of sulphur granules in the sputum.

The roentgen picture is not characteristic. Areas of consolidation may be present and in some instances there are localized nodules, as noted in the case report below. In those cases in which

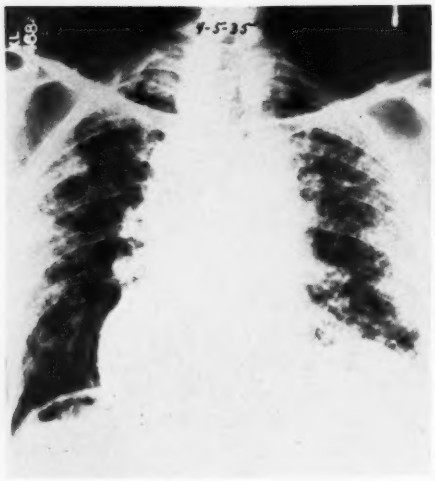

Fig. 3, Case 3.

pleural involvement is present, there may be fluid in the pleural cavity. Sometimes cavitation in the form of abscess cavities are seen.

The disease must be differentiated from tuberculosis, but in some cases it may simulate lung abscess, tumor, or empyema.

In practically all cases with pulmonary involvement, the disease ends in the death of the patient. Potassium iodide in large doses seems to be of considerable benefit. Surgical excision of localized lesions has been curative but this is scarcely applicable to pulmonary lesions. Roentgen therapy to such lesions, combined with potassium iodide and possibly vaccine, would seem to offer the greatest hope of success.

Case 2. White male, aged 17. The patient was admitted with a complaint of draining sinuses in the abdomen. He stated that he had been well until 11 months previously, at which time he suffered a ruptured appendix for which he had a subsequent operation. Six months later, intestinal obstruction developed, for the relief of which several operations had been performed. Three weeks previously an abscess in the left lower quadrant was opened; several of these openings were draining at the time of the examination. There was loss of strength and weight, and his appetite was poor. The temperature was only slightly elevated.

Physical examination revealed evidence of several surgical incisions with draining sinuses over the abdomen, in which several masses were present. The lungs were essentially clear.

Smears of pus from the draining sinuses showed evidence of actinomycosis.

Roentgen films of the chest disclosed a large, smooth, rounded shadow of increased density in the base of the right lung just above the diaphragm. In view of the abdominal actinomycosis, it was felt that this lesion had the same etiology (Fig. 2).

Roentgen therapy was instituted and carried out over a period of several months. This produced a remarkable improvement in the patient's general condition. He gained weight and strength, and his color and expression were considerably improved. The palpable abdominal masses almost disappeared. X-ray films of the chest at that time showed a diminution in size of the mass in the base of the right lung but not disappearance of it. The patient then left and we have been unable to trace him farther.

Moniliasis.—Attention was first directed to this condition by Castellani (3), in Ceylon, in 1905. It is now conceded that while *Monilia* may be the cause of primary bronchopulmonary disease, it may also be present as a secondary invader in cases of primary bacterial infection. *Monilia* is usually a saprophyte and is frequently found on decayed vegetable matter. In some cases it appears to be a harmless invader; in others it becomes pathogenic to either man or animal.

Two types of clinical cases are described by Castellani (3): a mild type and a severe type. In the mild type the patient exhibits few symptoms or signs. He may be ill a few weeks or months and clear up spontaneously, or the disease may continue into the severe type.

In the severe type the history suggests tuberculosis. There is weight loss, fatigue, fever, cough, and sometimes hemorrhage.

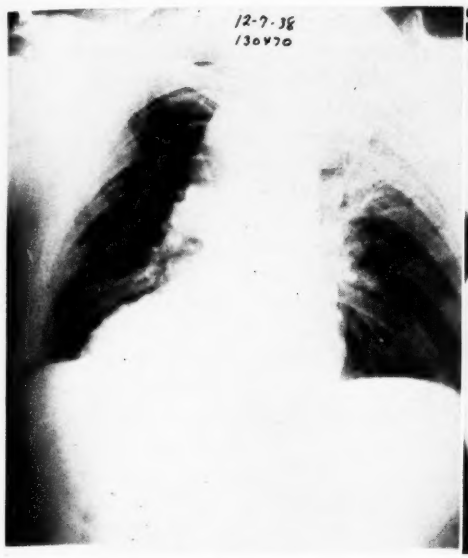

Fig. 4, Case 4.

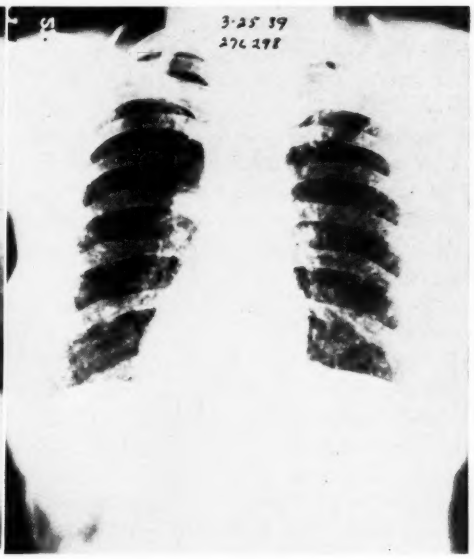

Fig. 5, Case 2.

Physical examination may reveal evidence of pleural thickening and sometimes consolidation. The apices of the lungs tend to be clear. Chronic cases may extend over a period of years, with omissions, but the acute cases often progress rapidly to a fatal termination.

The diagnosis of pulmonary moniliasis rests upon the constant presence of monilias in the sputum and the absence of tubercle bacilli. The sputum must also be collected with every precaution to avoid external contamination.

Roentgenograms of the chest show a variety of changes. There is usually a marked enlargement of the hilar areas, with extensive infiltration extending from these areas throughout the lungs. In some cases there is a patchy type of infiltration present in various parts of the lungs. This differs somewhat from tuberculous infiltration and is usually less marked in the pulmonary apices. There is generally an extensive fibrosis forming a network of infiltration throughout the lungs. There may be considerable studding along the bronchovascular markings. We had a series of five patients, all in one family, in which miliary changes were present throughout both lungs. These were somewhat coarser than the nodules of miliary tuberculosis but otherwise were similar. No tubercle bacilli were ever found in these cases (Fig. 5).

Postmortem examination usually shows replacement of the pulmonary parenchyma by a diffuse fibrosis. The bronchi may contain exudate which has many round and wandering cells. The actual monilia are usually present in large numbers. There may be small abscess cavities about the smaller bronchioles and these contain monilia.

Castellani (3) suggests the use of potassium iodide with which glycerophosphates and balsamics may be associated. He calls attention to the fact, however, that in certain instances potassium iodide is practically without beneficial effect. Vaccines may be helpful in some cases.

The following report is of a case of ours which came to the postmortem table.

Case 3. White male, aged 69. The patient came to the hospital complaining of weakness, cough, shortness of breath, and loss of weight. The symptoms were

first noticed six months previously, beginning with a non-productive cough, which later became productive of a white foamy sputum.

Physical examination disclosed an emaciated man 50 pounds underweight, coughing and expectorating. There was impairment on percussion over the upper chest. Bronchial breathing and showers of fine and medium moist râles were heard throughout both lungs. There was clubbing of the fingers.

The sputum was repeatedly negative for tubercle bacilli, and the tuberculin test was negative. The sputum culture showed the presence of *Monilia* repeatedly.

Roentgenograms of the chest disclosed evidence of hilar enlargement on both sides and an extensive network of fibrosis throughout both lungs. Some nodular development was present in both lungs. There was slight pleural reaction along the axillæ. The upper dorsal spine showed a mild degree of scoliosis and the trachea was displaced to the right side (Fig. 3).

Potassium iodide was administered but had no appreciable effect on the course of his illness. Death occurred three weeks after admission.

At the postmortem examination the following significant changes were found. The pleural surfaces were covered with a fine fibrous deposit, less marked over the apices. The hilar nodes were enlarged and on section were soft and deeply pigmented. The large bronchi contained a moderate amount of stringy, almost gelatinous, mucopurulent material. There was greatly increased density of the pulmonary parenchyma. The cut surface had a firm fibrous appearance and a mottled grayish-white color. There were multiple small areas of bronchiolar dilatation, scattered through the lungs and other small areas which suggested patches of bronchopneumonia. The consolidated process had somewhat the appearance of a caseous pneumonia but was firmer in consistency, dryer, and more fibrous in character. Bacterial examination of the sputum disclosed *Monilia*. Microscopic examination showed almost complete replacement of the pulmonary parenchyma by diffuse fibrosis.

Aspergillosis.—This disease is the result of infection by one of the *Aspergillus* fungi. It is frequently present in pigeons, and in some countries pigeon-breeders acquire the disease. It is not common in this country as a primary pulmonary disease but has been noted occasionally as a secondary invader in the course of other diseases.

Schneider (9) states that the onset of the infection is insidious. The symptoms are much the same as in tuberculous infection. There is often a productive cough with frothy purulent sputum. Hemoptyses are frequent. Schneider says that patients with this disease have a rather healthy appearance and do not look ill or emaciated, as they often do in tuberculosis and other chronic lung diseases.

The roentgen films of cases of primary pulmonary aspergillosis reported in the literature, have not shown any characteristic findings. There is usually evidence of fibrosis and emphysema, together with some pleural reaction. The picture is usually mistaken for that of tuberculosis.

Other filamentous fungi having characteristic fructifications which are of clinical importance are *Penicillium* and *Mucor*. These are often saprophytes and not primary invaders. They are often present on decayed vegetable matter and moldy hay. Fawcitt (5) has described numerous cases of workers with moldy hay, who showed severe clinical symptoms. He applied the name "bronchomycosis feniseciorum" to this condition. The first symptoms include increasing shortness of breath, cough with frothy sputum, and slight fever. The sputum usually contained a mixed infection of *Aspergillus, Penicillium,* and *Mucor*. He described the roentgen changes in four stages beginning with mild peribronchial changes, passing into mottling that may be mistaken for miliary tuberculosis. There is then enlargement of the hilar areas. Later there are patches

of increased density due to coalescent areas of fibrosis. There is restriction of motion of the diaphragm, emphysema, and cardiac enlargement.

This infection, he believes, may provide a soil for the development of such diseases as tuberculosis or malignant disease. Sayers and Meriwether (8) reported the discovery of fungi in the sputum of 31 cases of miliary lung disease with calcification. They were present in every case examined and consisted of several types of *Aspergillus* fungi. We have had one case of *Penicillium* infection which was probably not the primary cause of death.

Case 4. White male, aged 69. The patient was admitted complaining that five days previously he had become ill with chills and fever. There was a moderate cough which was productive of thick, grayish-white, mucoid material. The sputum was occasionally blood-tinged, but there was no frank hemoptysis.

Physical examination of the chest disclosed evidence of impairment over the chest posteriorly. Breath sounds were distant over the impaired areas, but there were no tubular breath sounds. Many yeast cells were found in the sputum. It was felt that this was an atypical case of pneumonia. *Pneumococcus*, Type VIII, was cultured from the blood.

Roentgen films of the chest showed evidence of extensive infiltration throughout the right lung, especially the right apex, with small areas of localized hazing suggesting bronchopneumonia. Fungous infection was suggested as a possibility (Fig. 4).

During the next few days the clinical condition of the patient became worse and the roentgen films showed progressive involvement of the lungs. He died on the fifth day of hospitalization.

Postmortem examination disclosed evidence of bilateral bronchopneumonia; bilateral acute bronchitis; fibrous pleuritis; calcified and caseous lymph nodes, right, and various lesions in other parts of the body. Cultures from the lungs resulted in the finding of *Penicillium*.

It was our feeling that the *Penicillium* infection was not the cause of death.

Coccidioidal Granuloma.—The infectious agent in this disease is the *Oidium coccidioides* which produces a generalized disease which may attack many of the bodily structures. It more commonly involves the skin, subcutaneous structures, glands, osseous system, and pulmonary structures. It is frequently primary in the pulmonary structures.

Nearly all of the cases have been reported from areas in this country west of the Rocky Mountains, but a few have been found in other parts of this country and South America. Most of the reported cases have been from California; we have no records of this disease in our files. Carter (2) has written an excellent report on this condition, deserving study by those interested in the subject, in which he describes the pulmonary lesions of this disease as consisting of extensive miliary lesions, nodular consolidations with caseation, massive consolidation, and abscess formation. By roentgen examination he found that approximately half of his cases, with pulmonary lesions, showed the miliary type of involvement. These miliary lesions appeared somewhat more obscure on the film than in corresponding cases of miliary tuberculosis. Considerable hilar enlargement was present in about 80 per cent of the cases; a mediastinal mass in about one-half. Some type of consolidation was shown by about 90 per cent of the patients reported. Little evidence of fibrosis could be seen from the films. A few of the cases showed evidence of pleural involvement, and several small cavities were seen in the upper lobes.

Treatment of these patients is far from satisfactory as no specific medication is available. Most of those with generalized infection suffer severe toxic prostration and death. The lesions resemble those of blastomycosis and tuberculosis.

Streptothricosis.—This is a relatively rare infection in man. Castellani (3) states that it is one of the most serious types of bronchomycosis, and usually ends

in death. There is weight loss, anemia, and sputum which is first mucopurulent and later blood-tinged. The physical examination may be negative or suggest scattered patches of infiltration in the lungs.

Singer and Ballon (10) have reported a case in detail, with a review of the literature. These authors believe the primary infection was in the lungs, but the fungus was found at autopsy in various parts of the body. There was fever, leukocytosis, and symptoms referable to the various affected organs. The lesions in the lungs showed extensive nodular infiltration similar to that seen in miliary tuberculosis. There was also evidence of necrosis and abscess formation. Tuberculosis was also present in the lungs, associated with it, and tubercle bacilli were demonstrated in direct smears from pus obtained from the abscess cavities, but had not been demonstrated in the sputum during life. In the differential diagnosis of streptothrix infection of the lungs, these investigators state that one must consider tuberculosis, actinomycosis, sporotrichosis, and glanders; also pyogenic lung infections.

We have had no streptothrix infections of the lungs.

DISCUSSION

It is self-evident from the above summary of the various bronchomycoses that there are no characteristic roentgen changes that will enable us clearly to differentiate these diseases from each other or from other diseases. There are, however, certain suggestions and also positive findings which may be obtained from a study of the roentgen films which will materially aid in arriving at a differential diagnosis.

The roentgen findings in all these bronchomycoses simulate, to some degree, pulmonary tuberculosis or some of its complications. In certain cases, bronchomycosis is suspected only because tubercle bacilli cannot be demonstrated after prolonged search for them, and because the clinical course of the disease is not typical of tuberculosis. Demonstration of the fungus will then lead to a correct diagnosis. Associated extrapulmonary lesions, such as skeletal lesions, fistulæ, and granulomatous skin lesions, are also an aid in directing attention to the search for fungi.

Some of the roentgen findings and their occurrence in the various bronchomycoses are miliary nodules. These are present in some form or other in all these diseases, except actinomycosis and aspergillosis. In the case of the latter, when it is combined with *Penicillium* and *Mucor*, as in hay workers, this is a prominent feature of the roentgen picture. In blastomycosis there is usually more fibrosis than in miliary tuberculosis. In certain cases of moniliasis there is studding along the bronchi and nodules which are usually larger and less discrete than those of tuberculosis (Fig. 5). Miliary nodules are also quite common in coccidioidal granuloma and streptothricosis.

Pulmonary necrosis with abscess formation is seen at some stage of the disease in a number of these infections. In blastomycosis, abscess formation is sometimes found, although in the case reported above this was not present. This complication is quite common in cases of actinomycosis and may secondarily involve the chest wall with the formation of persistent fistulæ. Small cavities may be present in moniliasis and coccidiosis but it is not a prominent feature of these diseases. Singer and Ballon (10) report abscess formation in their case of streptothricosis.

In many of these cases the occurrence of pulmonary fibrosis is the prominent feature of the lesion. It is well marked in the lesions of blastomycosis and may extend far up into the apices. In moniliasis there is usually a replacement of the lung parenchyma by a diffuse fibrosis. Fibrosis with an accompanying emphysema is seen in aspergillosis and penicillosis. It is present to some extent in the other bronchomycoses but it is not as prominent a feature of these diseases.

Pleuritic involvement, with or without

empyema, may be present in any of these infections and is frequently an outstanding feature of actinomycosis with secondary involvement of the chest wall. In nearly all cases reported with postmortem findings, there was evidence of pleural changes.

Areas of a patchy type of consolidation, similar to bronchopneumonia, are also present at some stage of the disease in most of these infections. Sometimes these lesions appear to represent areas of primary involvement which may coalesce and break down with the formation of abscesses. In other instances they appear to be due to a terminal bronchopneumonia which is often the direct cause of death.

Sometimes basilar involvement is more common than the apical involvement, which may be of value in suspecting nontuberculous infection. There is often considerable hilar enlargement and in coccidiosis there was a mediastinal mass present in almost half of Carter's (2) cases.

SUMMARY

The bronchomycoses, while not rare, are not discovered with great frequency, and until the past few decades comparatively little attention was devoted to them.

The symptoms and signs are similar to those of tuberculosis and often they are at first thought to be tuberculous in origin. Whenever the history or x-ray changes are atypical of tuberculosis, the sputum should be examined microscopically and also cultured repeatedly, so that these cases may not be treated as tuberculous cases.

In early stages, these patients appear to have a mild bronchitis with some expectoration; later they develop many of the signs and symptoms and even the complications of tuberculosis. The final diagnosis rests on the discovery and identification of the offending organism.

The roentgen changes are suggestive of a differential diagnosis in some instances but usually one can only suggest the presence of a fungus infection. We have attempted to describe some of the more prominent roentgen signs of the various bronchomycoses.

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DIFFERENTIAL DIAGNOSIS OF NON-SPECIFIC INTERSTITIAL PNEUMONITIS[1]

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THE terms "pneumonitis" and "pneumonia" are synonymous; both may be defined as "inflammatory disease of lung parenchyma." Many pathologists, however, reserve "pneumonitis" for use in designating pneumonia of the chronic interstitial fibroid type, which may be encountered under a wide variety of clinical circumstances. As a result, "pneumonitis" has acquired an implied limitation of meaning.

Although lobar pneumonia in its classical form is, strictly speaking, a form of pneumonitis, the distinctive clinical and radiologic features of this disease justify its specific designation as lobar pneumonia by the radiologist. Likewise, in the majority of instances pulmonary tuberculosis can be identified radiologically with a reasonable measure of confidence. It is only when the telltale signs characteristic of some particular pathologic process are lacking that the radiologist feels the desire to avail himself of the latitude which the widely inclusive term of "pneumonitis" implies.

Chronic inflammatory processes in the lungs are prone to result in fibrous scarring within the alveolar walls and about the bronchi. This state of affairs can be demonstrated microscopically in a number of situations, such as chronic fibroid tuberculosis, silicosis, and unresolved lobar pneumonia. Since it is by no means possible to differentiate the various disease entities which may be associated with this type of pulmonary inflammation on the basis of roentgen findings alone, it is both sensible and convenient for the radiologist to report findings which suggest chronic fibroid pneumonia as "interstitial pneumonitis," making no attempt to identify the etiologic factor unless circumstantial evidence of some sort is available to identify the causative agent. Because the various inflammatory processes which may affect the lungs are so variable in their radiologic expression it is extremely difficult, if not frankly impossible, to describe in terms of location, configuration, size, and relative density the various appearances which might be considered characteristic of non-specific interstitial pneumonitis.

If one were to use a process of exclusion, lobar pneumonia might be set apart because, if seen in relatively early stages, this disease produces almost uniform abnormal opacity of the lungs, sharply limited in at least a part of its periphery by the pleural surfaces of the involved lobe or lobes. The pneumonic lung under these circumstances frequently shows radiographic evidence of slight shrinkage. Periodic examination at relatively short intervals is very enlightening because the radiologic manifestations of the disease notoriously lag behind the clinical signs, and the entire process resolves and disappears in short order unless complications develop.

Lobular or bronchopneumonia presents a different radiologic appearance characterized by patchy abnormal density becoming confluent if the zone of involvement is sufficiently large. This form of pneumonia may be more widespread than is customary in the lobar type, though it is not uncommon to find the disease confined to a single lobe at any one time. Either of these types may involve multiple lobes or may progress from one part of the lung to another. All forms of pneumonia can be produced by a variety of organisms. As an example of one of the less common etiologic factors,

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the fusiform bacillus and the spirochete of Vincent may be cited. There is little in the radiologic appearance of pneumonias, in general, to indicate the identity of the causative agent. However, the time factor involved in the process of resolution as determined by repeated roentgen examination is sometimes of considerable assistance.

The aspiration of foreign substances into the air passages constitutes an insult to the lung which is commonly associated with inflammatory reaction. Aspiration pneumonia is not infrequent following general anesthesia and even after local anesthesia of the upper respiratory tract. Derangement of the nervous mechanism controlling the epiglottis and the muscles of deglutition may permit ingested materials to be aspirated into the chest with the resultant development of pneumonia. To cite a case in point, a zone of pulmonary inflammation was recognized deep in the right lower lobe of a patient subsequently shown to have an annular neoplasm of the esophagus producing relatively high grade obstruction and consequent spill-over of esophageal contents into the trachea and bronchi. The process had become chronic because of often repeated insult to the same portion of lung. The pulmonary lesion was not associated with the usual abrupt and alarming clinical manifestations of pneumonia.

Following the aspiration of solitary foreign bodies and even without the blockage of air supply to large areas of lung, the development of local inflammatory disease is commonplace. So long as the foreign body remains, inflammatory disease persists, ultimately becoming chronic with the production of non-reversible scarring.

Sometimes the resolution of acute pneumonia is incomplete. Reparative processes are interrupted by recrudescence and active suppuration may occur locally with liquefaction necrosis and abscess formation. Before an abscess cavity can be demonstrated radiologically, before evacuation of necrotic material has occurred, lesions of this sort are exceedingly difficult to identify, with certainty, on the basis of a single radiologic observation.

One of the most commonly encountered pulmonary situations, in which characteristic radiologic evidence can be obtained, is

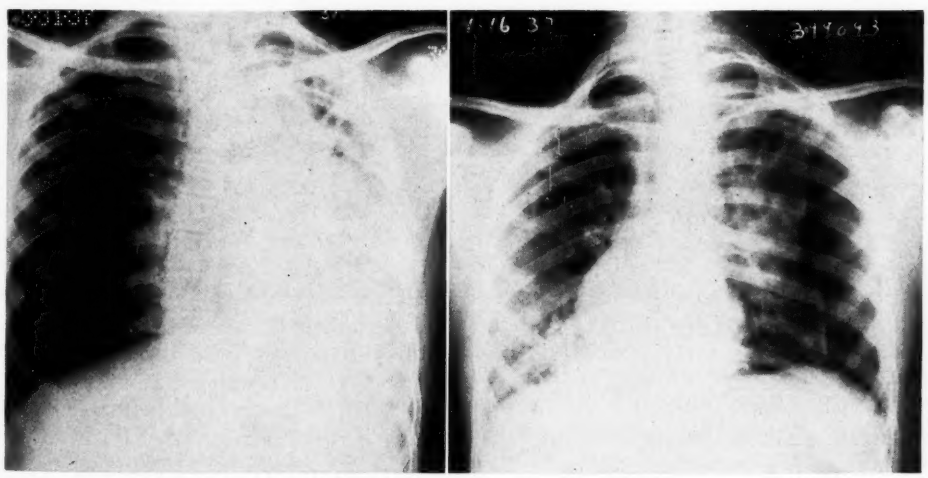


Fig. 1-*A*. Fig. 1-*B*.

Fig. 1-*A*. Colored female, aged 15 years. Atelectasis, mediastinal displacement, multiple cavities in the lung. Far advanced pulmonary tuberculosis with multiple cavities and scar-tissue contracture suspected.
Fig. 1-*B*. Same case following diagnostic pneumothorax, showing absence of extensive intrapleural adhesions. Multiple cavities in the lung. Ultimate diagnosis: obstruction of left bronchus by adenoma producing profound bronchiectasis and interstitial pneumonitis.

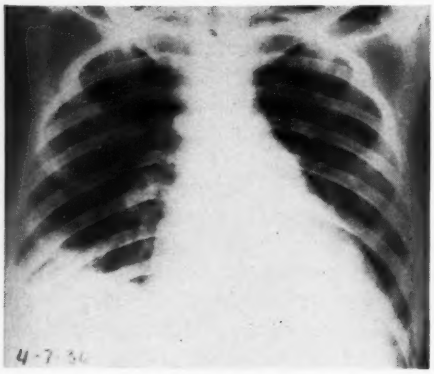


Fig. 2. Patchy pneumonitis representing actinomycotic pneumonia, confirmed at autopsy.

bronchiectasis. There is reason to believe that in a majority of these cases chronic interstitial pneumonitis precedes and, in fact, is instrumental in producing bronchial ectasia. Rarely, microscopic examination yields evidence of primary or congenital bronchial defects with superimposed inflammatory disease. One case in point might be mentioned in which, upon removal of the diseased lobe, the pathologist was able to demonstrate the widespread absence of certain elements in the bronchial wall. The existence of bronchiectasis may also be confidently suspected on the basis of radiologic evidence of interstitial pneumonitis corresponding in distribution to one or more of the major bronchi. It is not always possible to exclude the existence of bronchiectasis without recourse to bronchography. This is notably true even in the case of individuals in whom bronchiectasis is known to exist in the lower lobe of one lung, for example; for it is by no means an infrequent experience to find less extensive bronchiectasis in portions of another lobe, showing no signs of pneumonitis.

Pneumonoconiosis, whatever the irritative agent, presents, sooner or later, the microscopic appearance of chronic interstitial fibroid pneumonia or pneumonitis with characteristic whorl-like deposits of fibrous tissue. Striations within these whorls are usually to be seen in contrast to the hyalin changes which are common in tuberculous pulmonary fibrosis. Radiologically, the late stages of pneumonoconiosis are quite characteristic, rendered so by the tendency of multiple punctate opacities in the lung to coalesce at the level of the carina. Before this stage is reached, however, the lesions of silicosis can be closely imitated by a number of diseases of far different nature. It is well to remember that the radiologic signs which characterize this disease are produced by chronic interstitial pneumonitis which differs but slightly from the same condition which may be produced by a number of other factors.

Following therapeutic irradiation directed to the chest and adjacent structures, there may develop within that portion of the lung subjected to relatively great intensities of radiation a series of pathologic changes which, from the microscopic viewpoint, are again to be described as interstitial pneumonitis. In roentgenograms, the lesion is at first seen as a relatively uniform shadow with poorly defined margins. With the passage of time, these characteristics are supplanted by radiating strand-like shadows following the general course of bronchi in the affected area. If the injury to the lung has not been excessive, complete disappearance of the radiologic manifestations may be expected. Not infrequently, however, residual scarring can be recognized as a prominent aftereffect.

With the foregoing considerations as a background, it can be recalled from the experience of every radiologist that unusual manifestations of commonly encountered diseases and confusing radiologic findings in rare and unsuspected situations must be expected when accurate differential diagnosis is attempted. In patients presenting the classical story of cardiac failure and exhibiting unequivocal clinical signs, pulmonary congestion and edema as a result of circulatory embarrassment are anticipated and, therefore, easily recognized. Occasionally, degrees of circulatory failure capable of producing visible alterations in

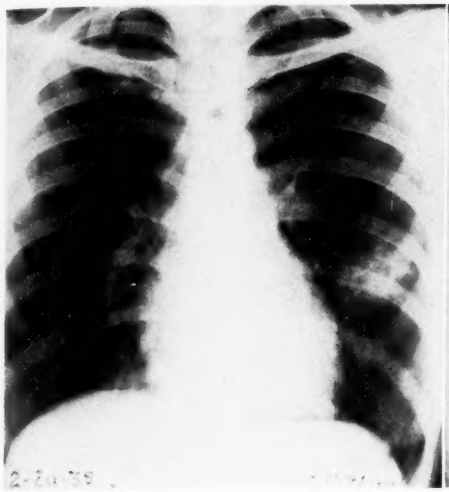


Fig. 3-*A*. Localized pneumonitis, left lung.

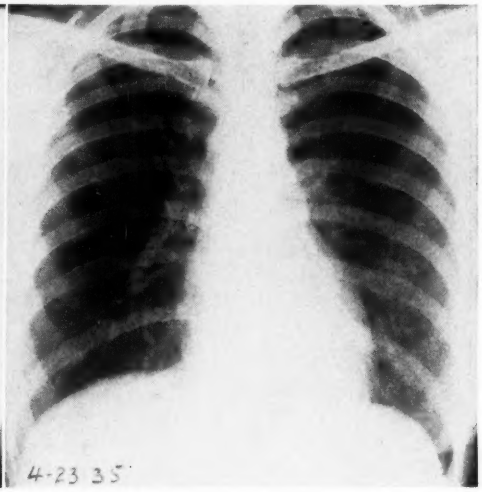
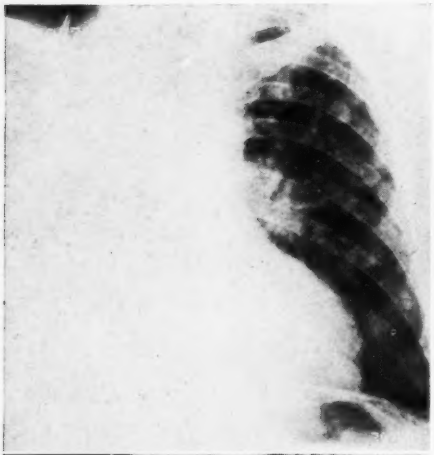


Fig. 3-*B*. Virtual complete disappearance following antisyphilitic therapy.

the appearance of the lungs are encountered by the radiologist, without warning. Under these circumstances, pulmonary edema and vascular congestion may be misinterpreted as evidence of inflammatory disease.

Long-standing bronchial obstruction with profound bronchiectasis of all lobes, produced by a small adenoma strategically placed in the left stem bronchus, produced in the chest roentgenograms of a 15-year-old negro girl, a very startling appearance. The heart shadow was lost in the generalized density throughout the left hemithorax and the trachea was sharply deviated to the same side. The contours of the diaphragm on the left and the left border of the heart could not be identified. In the upper portion of the chest and along the left axilla, definite signs of multiple cavities throughout the lung could be seen, leading to the initial impression of far advanced unilateral pulmonary tuberculosis with extensive cavitation and fibroustissue contracture. This impression was certainly strengthened by the age, sex, and race of the patient. Grid films of the chest, the entire absence of suggestive findings on the right, and the absence of confirmatory proof in the form of positive sputum analysis introduced doubt regarding the accuracy of diagnosis. Diagnostic pneumothorax proved the left lung to be entirely free from intrapleural adhesions, a situation scarcely to be expected in chronic fibrotic tuberculosis, and bronchography showed the imprint of the bronchial tumor in the column of iodized oil abruptly terminated in the left main-stem bronchus. After removal of the entire left lung, microscopic examination showed a profound degree of bronchiectasis involving all bronchi as well as far advanced, chronic, interstitial, fibroid pneumonia throughout the entire lung. This situation was scarcely to be expected on the basis of the initial chest roentgenograms (Fig. 1).

A patient desperately ill with high fever and definite clinical signs of widespread pulmonary disease presented radiologic findings difficult to explain. Irregular patches of abnormal density were to be found scattered throughout both lungs. These patches of abnormal density might have been considered as evidence of multiple pulmonary infarction or as widely separated zones of bronchopneumonia shortly followed by massive pleural effusion



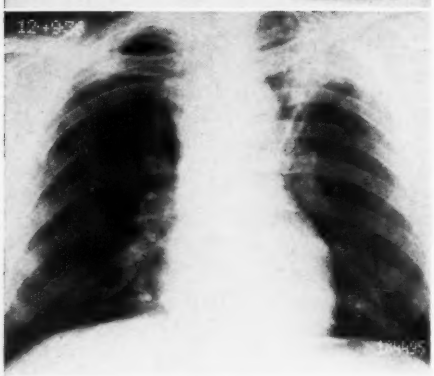


Fig. 4 (*above*). Bronchogenic carcinoma, upper lobe, right, with extension to other lobes of the same lung and pleura. Multiple metastases in the left lung.

Fig. 5 (*below*). Metastasis of squamous-cell carcinoma on dorsum of left hand to chest wall and lung, right apex. Radiation pneumonitis in axillary portion of the left upper lobe.

on the left. The patient continued on a rapid downhill course which was shortly fatal. At autopsy, widespread actinomycotic pneumonia was discovered and subjected to proof by morphologic and bacteriologic methods. In retrospect, the roentgenograms present no characteristics to warrant identification of the causative agent (Fig. 2).

In the case of a woman entering the hospital for the diagnosis and treatment of an open ulcerating lesion on the dorsum of one foot, radiologic examination of the chest—carried out as a means of weighing the likelihood of tuberculous etiology—showed a most unusual and highly localized though indistinctly outlined zone of increased density in mid-lung on the left. Certainly, this could not be considered characteristic of tuberculosis and was of necessity interpreted as "localized pneumonitis, etiology indeterminate." On dark-field examination a day later, spirochetes were identified in material taken from the ulcer on the foot and antisyphilitic therapy was at once begun. Closely paralleling progressive healing of the skin lesion, the abnormally dense patch of lung was observed to regain progressively its normal appearance, leaving no doubt as to its syphilitic nature (Fig. 3).

As a rule, pulmonary metastases from malignant neoplasms are seen in roentgenograms as sharply circumscribed, lobular densities buried in lung substance. This is not always the case, however, for rarely pulmonary metastases take the form of relatively small, flake-like densities of more or less uniform size which may easily be mistaken for evidences of silicosis, miliary tuberculosis, or other lesions of this sort. In one case in which this situation was encountered, the entire hemithorax on the right was largely obliterated as the result of a primary bronchogenic carcinoma in the upper lobe with direct extension and metastasis to the middle and lower lobes and the pleura, and with the further complication that the left lung was sprinkled with small granular metastases. Under these circumstances, far advanced pulmonary tuberculosis on the right, with subsequent miliary spread to the opposite lung, would certainly occur to most observers as the more likely explanation (Fig. 4). In another case under observation for a considerable period because of a large basal-cell carcinoma involving the dorsum of the hand, treated by amputation at the mid-forearm, re-amputation at a higher level with complete axillary dissection, and post-operative radiation, examination of the chest showed a smooth, hemispherical mass, close to the axilla high on the right, with underlying rib

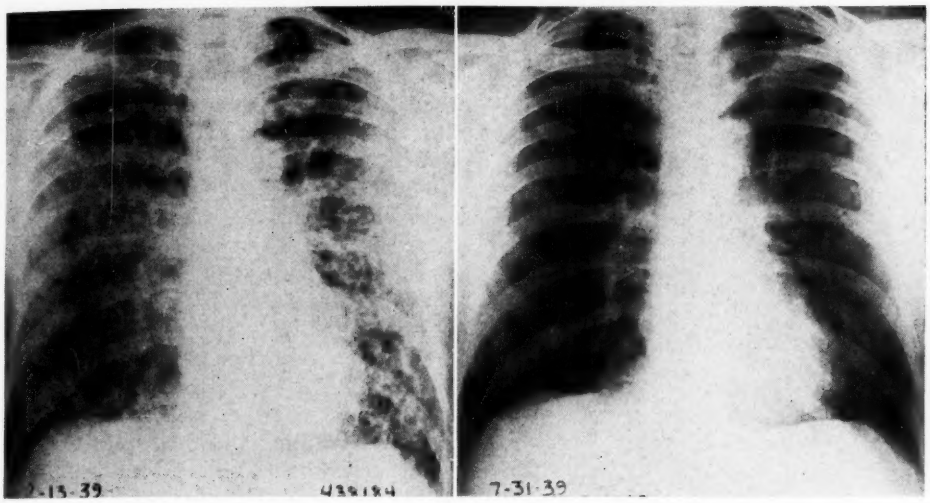


Fig. 6-*A*. Miliary type of pneumonitis in both lungs; diagnosis indeterminate.

Fig. 6-*B*. Rapid resolution following treatment for coccidiomycosis.

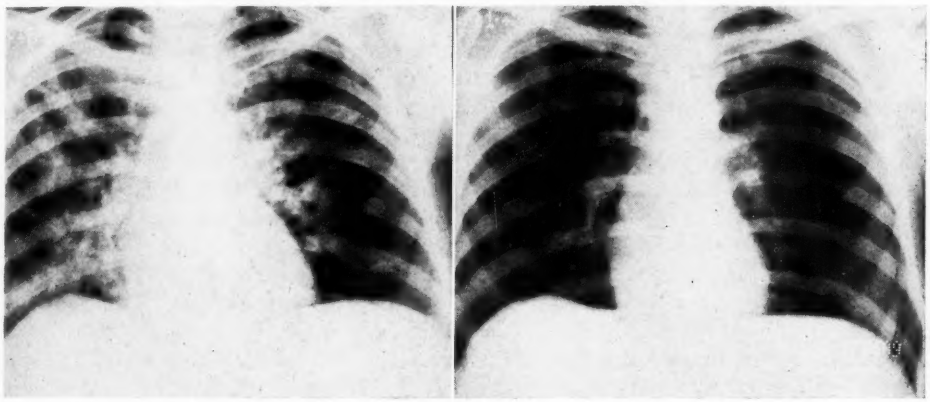


Fig. 7-*A*. Patchy pneumonitis, representing sarcomatous type of Hodgkin's disease.

Fig. 7-*B*. Same chest following radiation therapy.

destruction, and a lesion in the left apex highly characteristic of moderately advanced pulmonary tuberculosis. As a matter of fact, the apical lesion on the left represented nothing more than radiation fibrosis to be expected as a result of the heavy irradiation employed in attempting to control this rapidly fatal and unusually metastasizing squamous-cell carcinoma (Fig. 5).

Another patient subjected to examination, because of continued temperature elevation and symptoms related to the chest, presented a striking and appalling appearance of extensive miliary tuberculosis. Repeated sputum examination and the persistent search for stainable tubercle bacilli when extended to include the consideration of other causative agents resulted in the conclusive diagnosis of coccidiosis, which responded nicely to treatment (Fig. 6). The appearance of this chest,

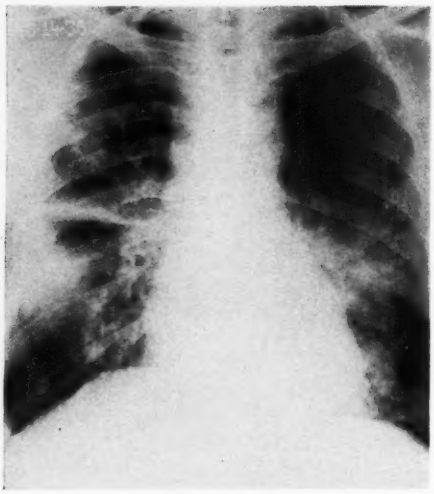


Fig. 8. Widespread bilateral pneumonitis and pleuritis. Leading occupational history. Diagnosis: pneumonoconiosis. Extensive Hodgkin's lesions in both lungs, hilum lymph nodes, spleen, and other organs were shown at autopsy. Also various stages of pulmonary tuberculosis and microscopic evidence of pneumonoconiosis.

when compared with that of another patient in which miliary tuberculosis was proved, provides no distinctive criteria upon which to base an accurate differential radiologic diagnosis.

The answer to the problem raised in another situation, in which peculiar splotches of opacity were observed scattered about throughout both lungs, was obtained as a result of microscopic examination of a palpable peripheral lymph node which showed unequivocal signs of Hodgkin's disease. By means of irradiation, the pulmonary lesions were caused to disappear quickly (Fig. 7). In another patient with a leading occupational history to indicate the probability of silicosis, this situation was diagnosed on the basis of punctate and coalescent opacities throughout both lungs with more pronounced and widespread pneumonic signs on the right. This patient shortly came to autopsy at which time Hodgkin's disease of an atypical form was clearly identified throughout both lungs, in bronchial lymph nodes, spleen, and numerous other localities throughout the body. In addition, there were definite evidences of pulmonary tuberculosis in various stages of the disease and in certain areas where the lymphoblastoma and the tuberculosis did not successfully obscure its characteristic signs, the typical arrangement of fibrous scarring seen in silicosis plus recognizable evidences of siderosis were observed and described by the pathologist (Fig. 8).

Summary.—Chronic interstitial pneumonitis is commonly encountered in radiologic examinations of the chest. The radiologic manifestations of this pathologic process may offer little evidence to suggest the particular causative agent. It is not at all uncommon that the etiologic factor may escape identification during the gross examination of pathologic material, and oftentimes the combined methods of physical diagnosis, radiology, pathology, bacteriology, and serology are required to identify the true nature of the disease. "Chronic non-specific interstitial pneumonitis" can be employed by the radiologist as a useful term to indicate that he has found what he believes to be evidence of long-standing inflammatory disease of the lung, the available characteristics of which will not permit more accurate classification.

THE MINIATURE X-RAY CHEST FILM[1]

By HOLLIS E. POTTER, M.D., *Chicago*, BRUCE H. DOUGLAS, M.D., *and* CARL C. BIRKELO, M.D., *Detroit, Michigan*

THERE have been many attempts to photograph the fluoroscopic image using both cinema and still camera methods, some of which have been to some extent successful. Growing out of the desire to provide a simple, inexpensive, and yet reasonably accurate method for the surveying of large numbers of individuals for the presence of tuberculosis or other diseases of the lungs, there have been developed several schemes for photographing the fluoroscopic image of the chest. De Abreu (1, 2), of Rio de Janeiro, should be given credit for having, in 1936, first applied such a method to surveys of large numbers, employing a contax camera for photography of the fluoroscopic image on 35 mm. film, the actual space used being 24 mm. These very small films can be economically taken but must, of course, be enlarged before they can be interpreted. Using this method, de Abreu and his associates have examined several hundred thousand persons and believe it to be practical for mass examination. They report being able to examine 1,000 persons per day with one machine. Janker (3) and Ulrici (4), as well as others in Germany have used this technic quite extensively and have reported favorably upon it.

Lindberg (5, 6), in this country, has adopted de Abreu's technic with some modifications of his own, and, while recognizing it as a cheap method for the examination of large numbers, in that it is more useful than the fluoroscope alone, believes that methods for the making of full size films should be improved upon rather than a definitely less accurate method.

Potter (7), a collaborator in this paper in consultation with the General Electric X-ray Corporation Laboratories, after much study and experimentation arrived at the conclusion that the most desirable objective in photography of the fluoroscopic image should be the production of a small film—small enough to constitute real economy in its use, and yet large enough to be readily interpreted without enlargement, or at least no greater enlargement than that provided by a simple reading glass. Working on this basis it was found that a 4×5 inch film with an effective focal range slightly smaller than this would answer the requirements. Special equipment was, therefore, designed for producing such photo-roentgenographs, and it is an evaluation of this method with which this study deals.

The technic of producing this film in our institution consists of the following factors: A modern x-ray installation with rotating anode tube capable of handling 400 ma. of current at from 60 to 80 kv., an impulse timer, and a tube–screen distance of 50 in. (or 125 cm.), thus producing as little distortion as possible. The time necessary for exposure depends on the thickness of the chest and varies from one-twentieth to four-twentieths of a second.

The fluorescent screen used is nearly seven times as fast as the usual Patterson screen. The lens is also a specially prepared instrument with a rating of F. 1.5 and is mounted in a tunnel with the screen at the opposite end so that both can be moved up and down to adjust to the proper level for a patient standing upright. This lens is capable of producing a sharp image in an area 3.7 inches in diameter on the 4×5 film. For the best possible results the patient's chest image must be within this area and, therefore, carefully centered.

[1] Presented before the Twenty-fifth Annual Meeting of the Radiological Society of North America, at Atlanta, Dec. 11–15, 1939.

In order to test the capacity of this 4 × 5 film, called the miniature film, it was decided to examine a large number of patients with both the regular 14 × 17 film and the miniature film, both to be taken at the same visit of the patient to the x-ray department. The regular film represents as nearly as possible the most up-to-date technic. It is taken at 72 inches tube–film distance, using a rotating anode tube, 400 ma., from 60 to 75 kv., and the time on an impulse timer varies from one-fortieth to one-twentieth of a second, depending on the thickness of the patient's chest from actual measurements with calipers. The upper limit of chest thickness which it has been attempted to ray is 30 cm. Patients who had previously had surgical procedures, such as pneumothorax or thoracoplasty, were also eliminated from this study. No other selection was used but most of the patients examined had symptoms of tuberculosis, were exposed to it, or had had a positive skin test. In this study 1,610 cases were so examined, an interpretation of the miniature film being always made and recorded independently and before a similar record of findings was made from the regular film, because the regular film was the standard by which the efficiency of the miniature film must be measured.

Name——————Date———Clinic No.——

0 No findings
0 Suspicious

0 Primary 0 A 0 B
0 Nodes 0 Paren.

0 Pleurisy
0 Dry
0 Wet

0 Minimal
0 Mod. adv.
0 Far adv.
0 Right lung
0 Left lung

0 Excavating
0 Exudative

0 Productive

0 Mixed

0 Apparently healed
0 Calcium
0 Fibrosis

0 Heart
0 Occupational

0 Non-tb. pul. dis.

Fig. 1.

TABLE I.—ACTIVE LESIONS FOUND IN 1,610 CLINIC ATTENDERS EXAMINED ON LARGE AND SMALL FILMS

Diagnosis from Large Film		Disagreement on Small Film	
		No finding	Inactive
Primary active	5	0	0
Pleurisy with effusion	17	0	1
Minimal active	117	5	3
Moderately advanced	92	0	1
Far advanced	40	0	0
	271	5	5

Five were straight misses, but of the five interpreted as inactive one was read "dry pleurisy," two "healed primary," and two "healed minimal." The two "healed primary" would not be re-checked, so they, with the five misses, make seven missed cases, or an error of 2.6 per cent.

For the interpretation of both films a simple card was devised which contained the outstanding points to be recorded. It is here reproduced as Figure 1. The major difficulty with this card is found to be that it requires rather definite classifications and does not provide for the many borderline conditions with which everyone is well acquainted.

A total of 271 patients were found to have active tuberculosis, including the primary type with lymph node enlargement, wet pleurisy, and minimal, moderately, and far advanced cases. In this group, that of primary interest, five of the minimal lesions were missed in the interpretation of the miniature films. Two other minimal lesions were called "healed primary." All of these lesions were very small and might easily have been missed in a regular film taken at a different angle, a slightly different depth of breathing, or with less perfect technic. In nearly every instance these missed lesions were superimposed over rib shadows in the miniature and not obscured in the regular film. Such small lesions may not call for immediate treatment, but should be watched and re-checked for possible changes. Granted that there were five completely missed lesions and two others called "healed primary," making a total of seven missed out of 271 active lesions, there is an error of 2.6 per cent.

The next small lesions to be considered are probably the active primary infection or enlargement of the lymph nodes. Five

such cases were found and none was missed in the miniature film.

The so-called dry pleurisies were made apices were centered nearer the middle of the film, throwing the bases out of focus. This has since been balanced so that the

TABLE II.—RELATIONSHIP BETWEEN READINGS OF A REGULAR X-RAY FILM AND A MINIATURE FILM FOR THE SAME INDIVIDUAL

Miniature x-ray film (horizontal columns)	Regular x-ray film (vertical columns) No Find.	Primary A	Pleur. Wet	Minimal Active	Mod. Adv. Active	Far Adv.	Other Lesions	Miniature Totals
No find.	782			5			107	894
Primary A		5						5
Pleur. with eff.			16				2	18
Min. active	3			106	9		2	120
Mod. adv. active				3	78	5	1	87
Far adv. active					4	35	1	40
Other lesions	42		1	3	1		399	446
Large totals	827	5	17	117	92	40	512	1,610

TABLE III.—RELATIONSHIP BETWEEN READINGS OF A REGULAR X-RAY FILM AND A MINIATURE FILM FOR THE SAME INDIVIDUAL

Other than active lesions

Miniature x-ray film (horizontal columns)	Regular x-ray film (vertical columns) No Findings	Suspicious	Primary B	Dry Pleurisy	Minimal Healed	Mod. Adv. Healed	Heart	Non-Tb. pul.	Fibrosis	Pneumothorax	Active	Total Miniature
No findings	782		80	9	7		1	6	4		5	894
Suspicious		1										1
Primary B	31		248		1		1				2	283
Dry pleurisy				43							1	44
Min. healed	2		1		17						2	22
Mod. adv. healed					1	7						8
Heart							10					10
Non-tb. pul.	2							30				32
Fibrosis	7		2			1			30			40
Pneumothorax										6		6
Active lesions	3			2	2	1			1		261	270
Regular film total	827	1	331	54	28	9	12	36	35	6	271	1,610

to include all the cases of old pleurisy in which only a small remnant, such as an obliterated costophrenic angle, was the remaining evidence. Of these, nine out of 54 were missed, an error of 17 per cent. This error is unnecessarily large and was greatest in the first group of patients examined because, in the attempt to make a definite recording of the very small lesions and knowing the prevalence of all tuberculous lesions in the upper portions of the lungs, too much concentration was given the apices. In other words, the bases are nearly as well demonstrated as are the apices, with the result that this error can be cut to a much lower percentage with little extra care.

The wet pleurisies included all cases of pleurisy which contained even small amounts of fluid, and none of these was entirely missed. One out of 17 such cases was called "dry" instead of "wet," so the error should not be considered serious.

On the diagnostic card there was no space set aside for "fibrosis of undetermined origin," so it was attempted to de-

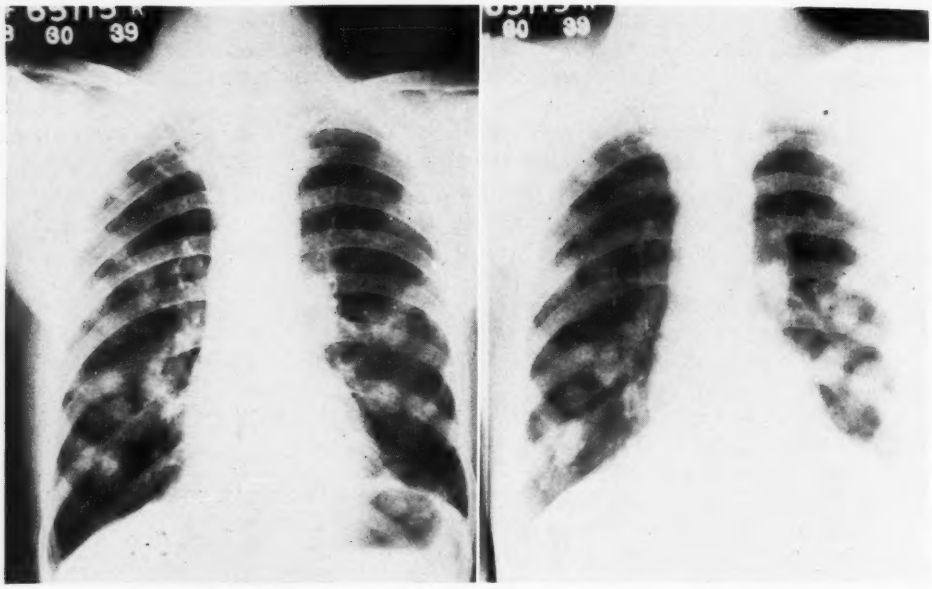


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Fig. 2. F-65115, Metastatic malignancy.

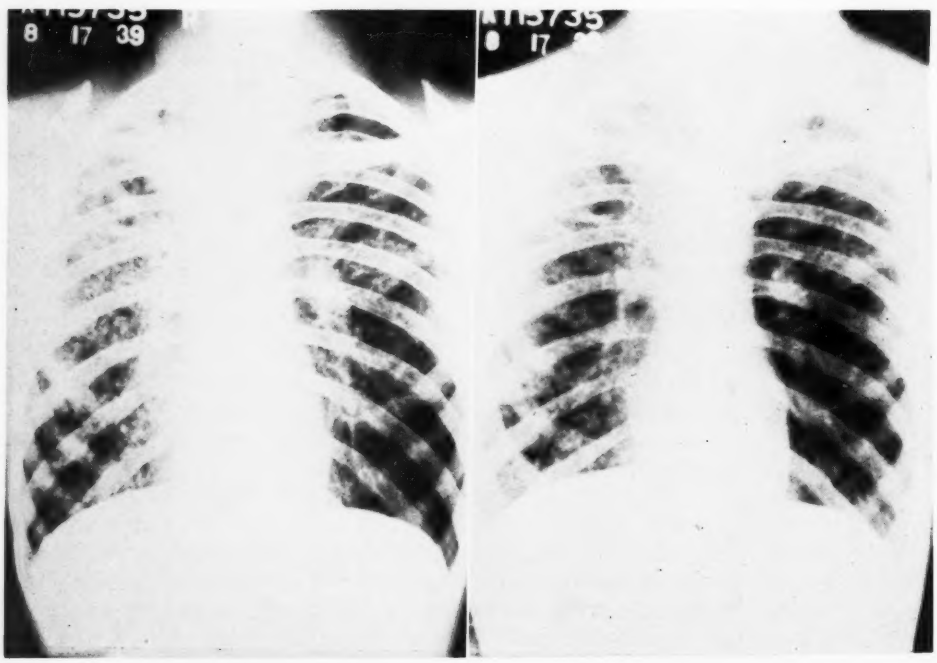

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Fig. 3. A-115735. Far advanced tuberculous lesion with excavation.

cide whether or not that was the result of tuberculosis or some other cause. That is not so easily done, even on the very best large chest film one can produce. From the regular films 28 such cases were classified as "minimal healed tuberculosis." Eight of these were not considered sufficiently significant, in the miniature film, to be mentioned: after a review of errors it is evident that these lesions have no clinical significance. If a descriptive report had been given, it is likely that no significant error would have resulted.

A fair number of the clinic patients were found to have valvular heart lesions from which symptoms often resulted, similar to those found in tuberculosis. The cardiac shadow in the small film is good because it is in the center of the film, where the greatest sharpness of detail is produced, but it was noticed that the heart shadow appeared enlarged in the small film. Therefore, rather than measure the diameters, particular account of the shape was taken. Two in 12 such cases were missed but, upon reviewing the errors, they were found to be entirely oversights because the findings were definitely there.

As regards non-tuberculous lesions and especially those at the base, the same things can be said about these conditions as were said about dry pleurisies. Some were missed at first, while too much concentration was given to the apical areas. Basal detail can just as well be obtained and its interpretation secured when one has learned to distinguish between shadow differences in the miniature and in the regular films.

In a critical analysis of any size of small film it must be remembered that both normal and abnormal conditions within the lungs are necessarily crowded into a smaller space and detail must of necessity suffer, whether one enlarges the film or views it as it is. It also naturally follows that the smaller the film the greater is this loss. An attempt has been made to demonstrate this point by making lantern slide reductions of both the regular film and the miniature film made of the same patient at the same visit to the department. However good the small film may be, it lacks the richness of detail of the regular film made with up-to-date equipment, as mentioned before.

Having established the reasonable accuracy of the method, it is now being

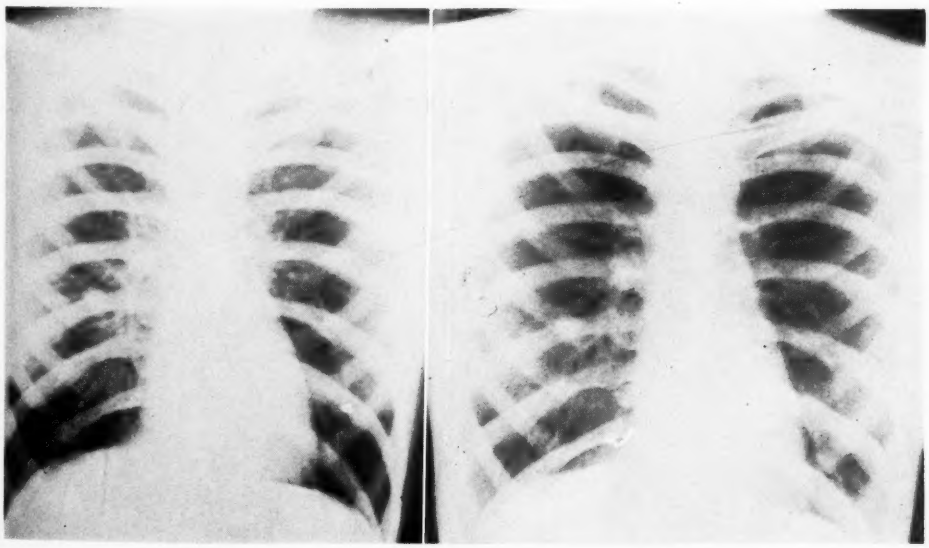

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Fig. 4. I-44473, Minimal tuberculous lesion.

applied to every new patient coming to the tuberculosis clinic, without the taking of a large film save in cases in which there is some questionable appearance in the small film. This has proven satisfactory in the two months this procedure has been followed, and obviously it is a great saving in film cost. There have been 1,719 persons examined in this group.

As a survey of presumably well persons who might have tuberculosis among their number, two groups are now being examined with the miniature film. The first is made up of the women attending the prenatal clinic of the health department. These are women unable to afford a private physician and, because of their age group and the fact that they are pregnant, it is important to examine them for tuberculosis—for their own safety as well as that of the expected child.

The second group of well persons being surveyed is made up of women who are employed on a WPA project in which the employees go out as housekeepers in welfare families where additional help in housekeeping is needed. It is important to examine these women to be sure that they are free of tuberculosis before they go to work in families with children.

A tuberculin test is being done on many of these women, using a single dose of 1 to 1,000 dilution intracutaneously, and all are x-rayed regardless of the result of the test. This will, in time, give valuable data on the value and accuracy of the prescreening with tuberculin. This will be reported in a later paper, since only 754 women have been examined so far, of whom four have been found with significant lesions.

In proposing this method of examination it seems that it can be carried out economically enough to make it possible to apply it directly in surveying large numbers without a preliminary tuberculin test, even in groups in which the reactor rate is low. In addition, there are certain inaccuracies in tuberculin testing, especially when only one dose is used, a 1 to 1,000 intracutaneous dose, or the von Pirquet, which approximates this dose in sensitiveness. In a recent study by Musacchio (8), an associate, in which he tested 1,000 cases of tuberculosis, it was found that, using a 1 to 1,000 dilution intracutaneously, there

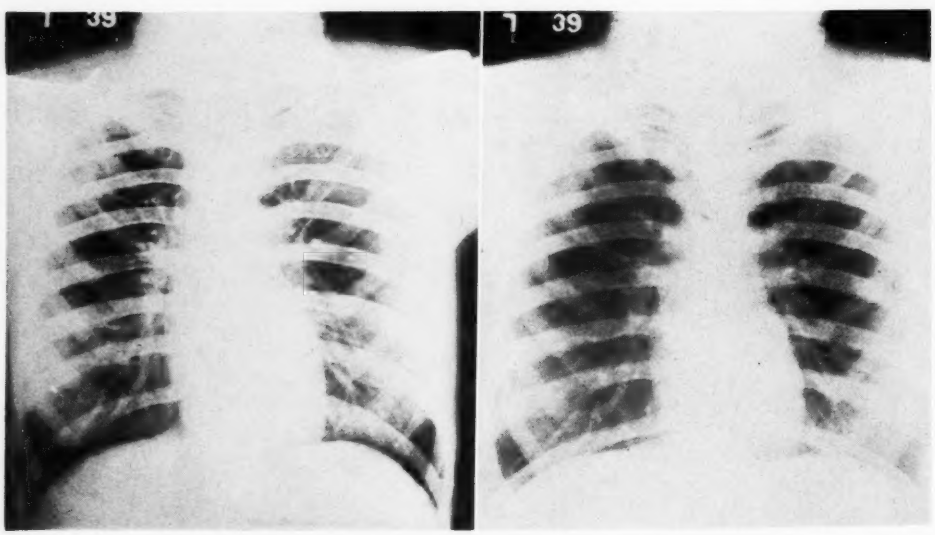

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Fig. 5. H-49931, Minimal tuberculous lesion.

were 847 reactors (or 84.7 per cent) and then, retesting with 1 to 100 dilution, there were added 122 (or 12.2 per cent) more. This is a significant number to miss with a one-dose method, and, of course, if a second test is given, it means extra effort and expense.

In using the x-ray alone there is need for only one visit by the patient, at which time the examination is made which results in a permanent record. In most instances this is complete, only a few patients needing re-examination; whereas with the preliminary tuberculin test, one visit is required to make the test, another for the reading, and if the two-dose method is used, still another visit is required before the x-ray is made. There is always a loss growing out of the fact that many reactors fail to appear for x-ray examination. This amounted to 4,719 out of 31,803 reactors (or 14.8 per cent), in a recent study in Detroit (9). Add to this the fact that most persons would rather have a roentgenogram taken than submit to a tuberculin test. There is also the possibility of the detection of other nontuberculous lesions of the heart and lungs which would be missed if only a tuberculin test were made. It is apparent, then, that there are several good reasons why a reasonably accurate but economical x-ray examination is better applied directly than when tuberculin is used as a preliminary screen.

The cost of taking the 4 × 5 inch film is very reasonable. In a test run 73 persons were x-rayed in 65 minutes, and the development of the films can be carried out as rapidly as they are exposed. To register, supervise the dressing room, place the patient, make exposure, and develop the film required the time of six persons.

The cost of a 4 × 5 film is approximately one-tenth of the cost of a 14 × 17 film, so it represents a very material saving. The tube cost for an exposure of a miniature film is nearly the same as the cost of exposure of a regular film when a rotating anode tube is used.

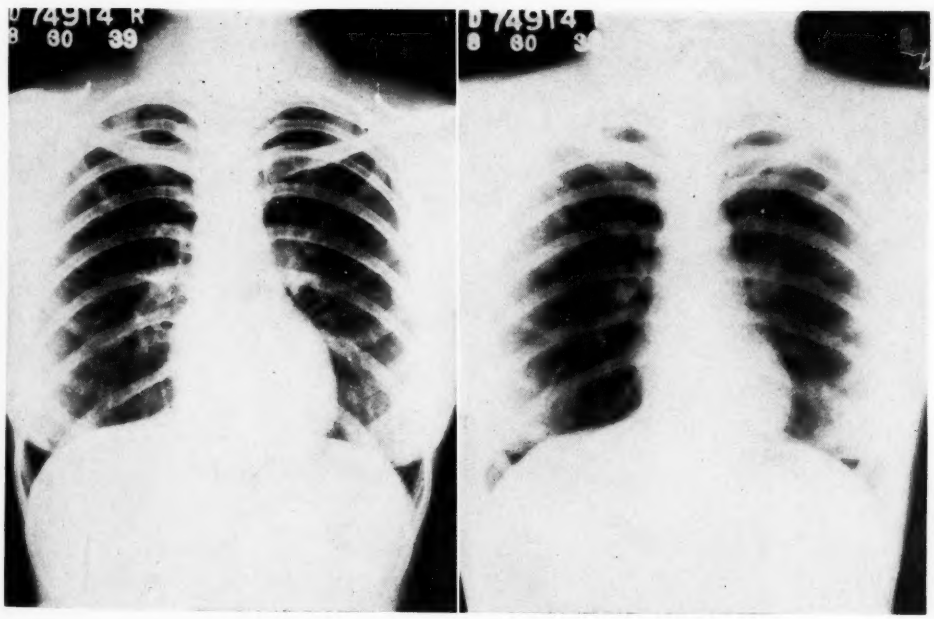

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Fig. 6. D-74914, Minimal tuberculous lesion—right.

These small films are easily handled, can be interpreted at the same speed as the large films, and require little space for storage.

To compare this method with other x-ray examination methods that may be used for direct survey purposes, there are four which should be considered.

First, full size celluloid film taken with a good technic is accurate but the cost makes it prohibitive for extensive use in large surveys.

Second, there is sensitized paper which, while reasonably accurate and about one-half as expensive in material cost as full size film, is still too expensive and is bulky to handle and store.

Again, the fluoroscope has been used extensively for surveys and, while quite inexpensive, its accuracy is open to some question, since no permanent record is made except in those cases referred for film examination.

Fellows (10) and his associates who have used the fluoroscope extensively and have made careful comparisons with well taken full size films found an error of 13 per cent in missed pulmonary tuberculous lesions in a series of 2,300 persons both filmed and fluoroscoped, taking the film as 100 per cent. The miniature film, 4 × 5 inches in size, can do definitely better than this.

Finally, the 35 mm. film, sometimes called "micro film," the actual field being 25 mm., while quite inexpensive to produce, is, in the opinion of many, too small. It must be enlarged either by projection or printing in order to permit of interpretation and in this enlargement considerable detail is lost. While this method has not yet been subjected to careful comparison for accuracy with full size film and with 4 × 5 inch film, some observation of its use suggests that too much has been sacrificed in accuracy in favor of economy, which cannot be said of the 4 × 5 inch film.

SUMMARY AND CONCLUSIONS

As a result of this study the authors believe they are justified in drawing the following conclusions regarding photoroentgenography with the 4 × 5 inch film:

1. This experience indicates that the

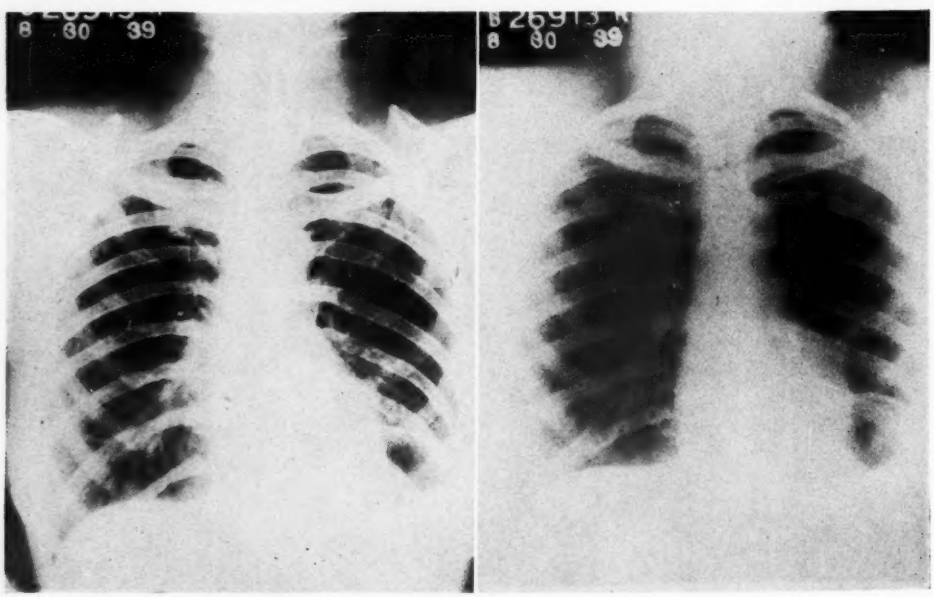

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Fig. 7. B-26913, Minimal tuberculous lesion—left.

4 × 5 inch photoroentgenograph is quite accurate. (Only 2.6 per cent error in detecting 271 cases with active tuberculous lesions as found in the full size film taken of 1,610 persons.)

2. This type of examination can be applied in survey work in tuberculosis to large numbers rapidly and economically. (Slightly faster than one per minute at a material reduction in cost.)
3. It has definite advantages over certain other x-ray methods of examination either in accuracy or in cost or both.
4. That this method of examination can be applied directly without preliminary tuberculin testing with greater accuracy and at the same time economically.
5. Finally, the authors believe photoroentgenography of this type offers a practical method for case finding in tuberculosis for use in surveying large numbers in susceptible groups.

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THE ROENTGENOGRAPHIC PROGNOSIS OF PULMONARY TUBERCULOSIS

By J. GERSHON-COHEN, M.D., *and* JOHN T. FARRELL, JR., M.D., *Philadelphia*

DESPITE the declining incidence of tuberculosis, the mortality rate continues to remain about the same. It has been estimated that approximately 50 per cent of the patients who develop clinical disease succumb, in spite of the aid of modern therapy. It is well, then, for the roentgenologist to investigate the prognostic possibilities of the roentgen examination of the chest which has now become a procedure of prime importance in the diagnosis of pulmonary tuberculosis. Can he foretell into which of the two groups, almost equally divided, any one case will fall? Immediately it becomes apparent that some standardization in diagnosis will have to be developed before any system of prognosis can be set up. To this end, the system of diagnosis adhered to, was arranged as follows:

THE ROENTGEN DIAGNOSIS

The essentials noted are:

1. Extent and distribution of lesions.
2. Type of lesions.
3. Cavities.

1. The extent and distribution of lesions are divided roughly into minimal, moderate, and widespread. Minimal, if less than two interspaces; moderate, about one lobe; widespread, if more than one whole lobe is involved.

2. The lesions are typed either predominantly as calcific, fibroid, exudative, caseous, or cavernous. When there are combinations of these types, the whole combination is listed in the order of their prominence, *viz.*, fibro-caseous, fibro-calcific, cavernous-fibroid, or caseous-cavernous, etc. The character of infiltration precedes the designation of the type, being described as diffuse, dense, linear, or discrete; if discrete—whether miliary, submiliary, acinar, acino-nodose, nodular, tuberculomatous, patchy bronchopneumonic, or lobar. This will thus result in such designations as a "minimal linear fibroid" infiltration, or a "moderate disseminated bronchopneumonic exudative," or a "widespread submiliary fibro-calcific infiltration."

3. Cavities receive special diagnostic consideration. The diameter is measured. The character of the walls and of the perifocal reaction is studied to learn whether exudation, caseation, or fibrosis predominates. Other important diagnostic criteria to be appraised are the completeness of drainage from the cavity, the extent of symphysis of the cavity wall with the parietal pleura, and the location of the cavity with relation to the lobes. These facts are often ascertained only from many films made with different angles of projection. It is sometimes even necessary to wait until after pneumothorax before arriving at a final conclusion.

ROENTGEN PROGNOSIS

After this methodical recording of the roentgen diagnosis, a prognosis is made, according to the following system. The forecast is limited to each lung separately; the changes on one side, however, bear on those of the other side in a given relationship worked in as part of the system.

BENIGN GROUP

Benign 4. The lesions are *most benign*, healed, or shall heal within four months.

Benign 3. Not quite *most benign*, and

[1] Presented before the Twenty-fifth Annual Meeting of the Radiological Society of North America, at Atlanta, Dec. 11–15, 1939.

the lesions shall heal within eight months.

Benign 2. Not quite *least benign*, and the lesions shall heal within 12 months.

Benign 1. The lesions are *least benign* and take as long as 18 months for complete resolution and organization.

VIRULENT GROUP

Virulent 1. These lesions are *least malignant* and heal within 18 months.

Virulent 2. Not quite *least malignant* and healing occurs within 24 months.

Virulent 3. Next to *most malignant* and healing may take 36 months.

Virulent 4. These lesions are *most malignant* and are hopeless, except in those cases in which surgical intervention may be successful. The remainder either terminate as so-called "good chronics" or die within a few weeks or months with terminal manifestations of the disease.

Benign 4.—These lesions are minimal in extent, fibroid or calcific. The distribution may be linear or discrete. In some cases, only some thickening of the pleura or pleuritic adhesions may be present in the later stages, or a simple idiopathic pleural effusion may be the only manifestation. These patients present few clinical symptoms, most of which are only suggestive; such as fatigue, failure to gain weight, or other such clinical symptoms of tuberculosis. There is no cough or expectoration. If sputum is present, no tubercle bacilli are found. In many cases, one sees only a few residua of hematogenously spread tuberculosis in which complete screening has taken place in the pulmonary capillary bed. This form may often be regarded as part and parcel of the primary complex, even though the earmarks are those of re-infection. It is usually impossible to be sure when the changes occurred with relation to the primary infection.

Benign 3.—This resembles the Benign 4 classification, but the lesions are more extensively disseminated, either in a localized portion of a lung or scattered throughout both lungs, but never involving an area greater than that covered by two interspaces. These lesions, too, are often the residue of a hematogenous spread of the limited, protracted, and disseminated types. Fibrosis and calcification predominate. There are practically no chest symptoms and if cough is present, it is usually nonproductive. A few suggestive symptoms, such as fatigue or underweight, may be present.

Both Benign 4 and Benign 3 are to be considered pre-clinical phases of adult tuberculosis and are often regarded as manifestations of the primary infection or of the second stage of hematogenous spread, organization of which is moderately advanced.

Benign 2.—Here, the lesions are minimal in extent, predominantly fibroid, either linear, fine-grained, or discrete in type. While the sputum is negative for the presence of tubercle bacilli, some definite clinical symptoms or signs of tuberculosis have developed, usually hemoptysis, fever, râles, and a slight increase in the blood sedimentation rate. This state is to be regarded as the earliest and most benign form of clinical adult phthisis in which recovery, by rest alone, is the rule within 12 months.

Benign 1.—This is like the preceding stage except that the lesions are more extensive, but do not exceed a moderate degree. Not more than the total area of one lobe is involved in the postero-anterior film. Fibrosis, though not necessarily organized, predominates. The linear fibrosis is not so fine-grained as in Benign 2. The discrete lesions are also fibrous, but not organized. *No cavities* are present in this group and the sputum must be scant, containing few, if any, tubercle bacilli. The clinical symptoms may be definite, but not marked. While clinical adult

tuberculosis is well established in this stage, very little bronchogenic spread occurs; no caseation or cavitation develops and, with absolute rest, the lesions show a tendency to heal usually within one year, but at the outside in 18 months.

The benign forms are thus split into two sections: the pre-clinical and clinical forms of tuberculosis, but all four groups are essentially of the fibroid type.

Virulent 1.—In this stage, the lesions are still minimal in extent but, though predominantly fibrous, evidence of proliferation, exudation, or caseation is already present. There are no cavities present. Bronchogenic spread may have occurred. Bacilli may occur in the sputum, but not in excessive amounts. The clinical symptoms are of recent origin and the patient has a good chance of recovery, with conservative treatment, within 12 months, although organization of the lesions may take 18 months.

Virulent 2.—This resembles the above stage, only the lesions may be moderate in extent and a cavity less than 2 cm. in diameter may be present. While some fibrosis may exist, exudation or caseation predominates. Into this group are also placed those cases of widespread involvement, if most of the infiltration is fibrous. The symptoms are of recent origin, and not more than six months in duration. Possibly 50 per cent of these patients will get well on conservative measures and this presumes disappearance of the cavities. A good portion of the other 50 per cent get well by pneumothorax or surgical intervention, if begun without much delay. These cases have full-blown symptoms and signs of fibro-cavernous tuberculosis or caseous-cavernous tuberculosis. Healing is expected to take place within 24 months.

Virulent 3.—These cases actually fall into the far advanced group, and could be regarded frequently as terminal were it not for the advantages of pneumothorax and the newer surgical procedures now available. Some few of these cases heal with conservative therapy and a small percentage become "good chronics." In all cases of this group, the phthisis is well established and well organized, the usual appearance is that of a diffuse exudative cavitary phthisis. The cavity is not over 5 cm. in diameter and if there are multiple cavities, their combined volumes should not exceed that of a cavity 5 cm. in diameter. Areas of exudation or caseation are irregularly distributed in the parenchyma, but evidence of exudation or caseation is always present in the perifocal areas about the cavities. If no cavities are present, but if there is widespread involvement of the lungs, even if an exudation or caseous response is present in only a few lesions or places, then such cases are also classed in this group. The sputum is usually, but not always, heavily positive. The pleura is often thick and involved with many adhesions so that when pneumothorax can be done, it often interferes seriously with compression of the cavities. Other surgical measures must be resorted to, and it is only because of their effectiveness that these cases are put in this category instead of being placed in the next or most virulent group. To prevent confusion, it should be restated that in the presence of excavation, the extent of parenchymatous involvement must not exceed a moderate degree, the only exception being those cases in which *no cavities* are present when the involvement of the parenchyma may be widespread and extensive.

Virulent 4.—All the so-called hopeless cases fall into this group, in one of three ways:

(*a*) A large chronic fibrous-walled cavity (over 5 cm. in diameter) may be present which can be dealt with only by thoracoplasty and, even then, not always successfully.

(*b*) The cavernous lesions may be so old and well established that even when they do not ulcerate with progressive enlargement, at best they remain almost stationary, the case coming under that heading designated as a "good chronic."

(*c*) The lesions may be so widespread, exudative, or caseous in nature as to leave

no doubt of the terminal nature and outcome of the disease.

Re-classification of Bilateral Lesions.—The above classification holds when only one lung is involved and this must be constantly kept in mind. When bilateral lesions are present, automatic shifts take place in this classification; by this is meant that the prognosis is worse and is so indicated according to a prescribed method of re-classification.

BILATERAL BENIGN LESIONS

1. If the original prognosis falls into the benign group on both sides, a shift to the left is made for each side. For instance, if the prognosis is Benign 3 right and Benign 2 left, then the final classification becomes Benign 2 right and Benign 1 left.

VIRULENT ON ONE AND BENIGN LESION ON THE OTHER SIDE

2. If the lesions are virulent on one side and benign on the other, then the benign designation, no matter of what grade, automatically becomes Virulent 1, but there is no change made in the original virulent designation of the other side. For instance, if the prognosis is Virulent 2 on the right and Benign 3 on the left, then the new classification becomes Virulent 2 on the right (unchanged) and Virulent 1 on the left.

BILATERAL VIRULENT LESIONS

3. If the lesions are in the virulent category on both sides, the shift to the left is done by adding the grade of the contralateral side to the original grade. For instance, if the classification on the right is Virulent 2 and on the left Virulent 3, then the final grading would become Virulent 5, but since these totals exceed 4, we simply call each side Virulent 4. If the total of both sides is less than 4, the simple totals hold. If the totals are exactly 4, we allow this to stand if this hopeless prognosis seems warranted by the clinical picture, but if the clinical picture is more favorable, we allow these cases to fall back into Virulent 3 for each side.

The technical exceptions for re-classification are very important and must be followed rigidly if good results are to be expected from this system.

COMMENT

Over 600 cases have been analyzed at the Eagleville Sanatorium, Eagleville Dispensary, and White Haven Sanatorium and the preliminary estimate reveals that our prognoses were correct for approximately 80 per cent. And, in order to limit the analysis as much as possible to the roentgen examination, the clinical picture and laboratory findings were excluded from all prognostic considerations. We believe, therefore, that when the same cases are reviewed to include these additional data, a better average of accuracy will be achieved.

Our best prognoses were made in the more advanced benign and virulent groups. In the Benign 1 and Virulent 1 groups, our failures were more pronounced, but it so happens that in our material, the smallest number of cases fell into these groups. Our good general average of accurate prognoses was thus little influenced. In the sanatoria, most of the cases were benign or virulent to a moderate or advanced degree, but, to our surprise, the same held true essentially in the dispensary practice. This would seem to indicate again that by the time the roentgen examination is asked for, pulmonary tuberculosis has passed beyond the early stages in which event none of us, the roentgenologist included, can foretell from a single examination which way the disease will progress. Resort to serial examinations can be made, however, and a fairly accurate prognosis arrived at in a few weeks. The statistical analysis of this work is to form the basis of a separate report to be given at an early date.

DISCUSSION OF SYMPOSIUM ON CHEST EXAMINATION

MERRILL C. SOSMAN, M.D. (Boston): I would like to congratulate the Society on this symposium which has been interesting and, I am sure, valuable to all of us.

With your permission, I would like to discuss these papers in the reverse order, taking the last one first, then going backward to the original paper.

I feel, in the first place, that I am the wrong man to discuss the last paper on the prognosis of tuberculosis. Most cases of pulmonary tuberculosis I see are sent to the various sanatoria in New England and I do not get a chance to follow them up, so my remarks on prognosis are not based on experience but are based on *a priori* reasoning.

I would like to object to one term in the last paper and that is the use of the word "malignant" in qualifying a form or type of tuberculosis. I do not think tuberculosis should be considered malignant. I do not know that "virulent" would be any better. Perhaps "favorable" or "unfavorable" might be better.

In the second place, as far as I am concerned, I find this classification more confusing than helpful. It looked rather simple as long as they talked of one lung but when the patient got bilateral lesions and the authors began adding 1 or subtracting 2, my concepts began to get more confused than clarified by the complex classification.

In the third place, I do not believe it is quite fair to give a definite prognosis based only on the extent or character of the lesion as revealed by x-ray because, I believe, there are a great many factors that affect the prognosis which are not visible on the x-ray film.

All of you know, I am sure, that tuberculosis in a Chinaman or in a negro or in a patient who has diabetes is quite a different problem from tuberculosis in the ordinary white individual who has a fair degree of resistance to the disease.

You all know, too, that basal lesions in adults are definitely worse than apical lesions, and apical lesions in children are definitely more serious than basal lesions, regardless of the extent of the involvement or of its character.

We have thought, in our experience, that an individual with vascular hypotension has definitely a worse prognosis than a similar patient with the same degree of involvement and the same character of involvement with normal blood pressure, and if there is a slight vascular hypertension we feel that the prognosis is definitely more favorable so that blood pressure—or perhaps that indicates a particular type of patient—may influence the prognosis considerably.

The apical lesions above the clavicle, we feel, are definitely more favorable than those in the subclavicular region, even with the same degree of involvement, and finally, on this particular paper, I think that serial films are by far the most important method of judging prognosis by the course of the disease in that particular individual.

Dr. Birkelo, in his paper with Dr. Potter and Dr. Douglas, has presented a very accurate and inexpensive method of surveying large groups of individuals for pulmonary disease. His error, I think, is extremely small—2.6 per cent as compared with 13 per cent by fluoroscopy alone or 16 per cent by skin tuberculin testing in dilutions of one to one thousand, the so-called "screening method," which, I think, is a snare and a delusion and should be abandoned.

Analysing his figures as presented here, we find that the error of this method in minimal tuberculosis is actually higher than 2.6 per cent; it is 4 and a fraction, as five cases out of 117 were missed by the miniature film. Even that is considerably better than any other procedure you might use in what is termed a "cheap" method.

The object of this type of survey is to do as good a job as possible at the minimum of expense, and I feel that this has been very well accomplished.

This type of examination will probably be limited to large cities or industrial communities, where large groups of individuals are to be examined at as low a per capita expense as possible. With that in mind, I feel that most of us in the country towns like Boston won't have to worry about it.

Dr. Needles[1] had a very interesting differentiation of pneumonia from pneumonitis by the failure of the latter to respond to sulfapyridine therapy—a fair method of analysis and useful in prognosis as well as in differential diagnosis.

Dr. Hodges had the usual very amazing and almost encyclopedic collection of unusual cases which I would not classify as pneumonitis any more than he does. He showed them, I think, simply to illustrate the difficulty and confusion in differentiating various types of lesions which we see in the roentgenograms of the lungs.

"Pneumonitis" should be used only in those cases of pulmonary inflammation which are non-tuberculous, which are not pneumonia—frank lobar or bronchopneumonia—and which have no known or obvious etiologic agent. You can use a qualifying term for the other groups. For instance, "post-irradiation pneumonitis" is perfectly acceptable and quite logical. The various types he showed—tumor, silicosis, irradiation reactions—can all simulate pneumonitis but, I am sure, he would not call them "pneumonitis" except by qualifying them by specifying those etiologic conditions.

As he said, obscure cases require a long and thorough study with the combined efforts of many men—clinicians, bacteriologists, serologists, micrologists, even the chemists at times—to make the differential diagnosis.

In our department and in our reports we use "pneumonitis" to mean something atypical, probably inflammatory, but with no known or obvious etiologic factor, and it usually refers to an organizing or chronic inflammatory process, so that most of our reports will read, "A chronic interstitial pneumonitis of unknown etiology."

Perhaps the most interesting paper of all, to me, was the one by the Chairman, Dr. Doub, and being a classmate of his and a very good friend, I am sure he will not mind if I pick on him a little bit. There are two things to be differentiated at once—the incidence of fungus infection and the clinical importance of that infection.

Norris, in his analysis, reported yeasts in the sputum of 15 per cent of all patients in the tuberculosis sanatorium in which he studied at that time; so that the incidence of fungi in the human lung is probably very much *under*estimated. The other point I would like to make is that, to me, the importance of this finding is very much *over*estimated. With few exceptions, I think, the fungus infection in the lung is secondary, saprophytic, and comparatively unimportant. Fungi are usually secondary invaders in such things as carcinoma of the lung, tuberculosis, particularly if there is a cavity, or even more commonly in bronchiectasis.

I would like to point out a fallacy uttered by our friend Dr. Fawcitt who presented a very good paper about two years ago at the International Congress on this subject. He made this ambiguous—or perhaps erroneous—statement: "Fungus infection may provide the soil for tuberculosis or malignancy." That, to me, is definitely putting the cart before the horse. I think the answer there is that the patient has tuberculosis or malignancy in the lung and the fungus is purely a secondary infection.

The exceptions, of course, are, first, actinomycosis, uncommon enough, fortunately, so that we rarely consider it. A severe chronic pulmonary infection, particularly with pleural involvement, should make one consider actinomycosis. If there is a chronically draining empyema cavity in addition, you should consider it three times instead of once.

Second, blastomycosis is even more rare. I do not believe we have a single case in our records.

[1] Paper not sent for publication.

Dr. Chamberlain knows all about the third exception, coccidiomycosis. Fortunately we do not have that in New England: I do not believe Dr. Doub had any in his group of cases. It is interesting to note the great number of cases which have been reported recently as "valley disease" which are, as far as I can learn, cases of pulmonary coccidiomycosis which have an acute onset, a short course, and complete recovery. A similar infection with a similar organism when there are also bone, skin, or gland lesions is usually fatal. Why you get that wide variation I do not know.

Finally, the monilia which has been emphasized repeatedly as the cause of pulmonary disease has, in our experience, invariably been the secondary invader. We are unable to find a single case which had monilia in the sputum that had not an underlying lesion such as carcinoma of the lung, bronchiectasis, or tuberculosis which could perfectly well explain the presence of a secondary saprophytic invader.

Aspergillus, I believe, causes little in the way of symptoms. Two of the United States Public Health men in Pitcher, Oklahoma, reported 120 cases of what was presumably a healed aspergillus infection in the lungs of miners, and they could not obtain a history of any illness in the majority of these men. The "pigeon breeder" who gets this disease should read, I think, "pigeon feeder," because in the Rhineland of Germany men have a very unhappy type of occupation in stuffing squabs for market. They take young pigeons and to get them fat rapidly, these men chew up grain, masticating it to a soft consistency, and then force it into the squab's beak with their lips, so the "pigeon feeders" get this disease rather than the "pigeon breeders." I do not believe any of our people here in the States will get pigeon feeders' disease.

Finally, I would like to interpolate a word about discussions. Too often there is not enough time available for discussion. Honest criticisms and frank differences of opinion often crystallize one's ideas and may add considerably to the value of a presentation such as this series of papers. I apologize if I have hurt anyone's feelings; there is nothing personal in my random remarks. The *argumentum ad hominem* must always be avoided in these meetings. May I compliment Dr. Doub on the symposium which he has arranged.

COL. ALBERT BOWEN (Fort McPherson, Ga.): We have been much interested in the use of the term "pneumonitis" to designate an acute, contagious form of respiratory disease manifested by fever, leukopenia, malaise, etc., usually quite mild, with definite, circumscribed x-ray evidence of exudation and possibly infiltration.

Since we first reported epidemics of acute influenza pneumonitis, in Hawaii, in 1934, there has been an increasing number of reports of epidemics of "benign," "circumscribed," "leukopenic," "atypical," "virus," and "interstitial" pneumonitis. Each reporter has chosen his own modifying term and they all seem to apply to this disease.

Those who have seen these epidemics are convinced that the disease is a clinical entity. Those who have seen only films of the cases say it is just a respiratory infection or bronchopneumonia. I have received personal communications reporting epidemics which have not appeared in the literature. Baylor University Hospital had an epidemic of some sixty cases, over a year ago, which has recently been reported in the *Texas State Jour. Med.* Wingfield, at Antioch College, has observed pneumonitis cases for several years and makes the interesting report that there is no change in the incidence of this acute benign pneumonitis during the influenza epidemics which occur from time to time.

The dispensary staff, at Cornell University, reported in the *Jour. Am. Med. Assn.*, last May, their experience with epidemics of what they termed "acute interstitial pneumonitis," thus being at variance with Dr. Hodges' definition of

interstitial pneumonitis as being only chronic.

We have been inclined to agree with Reimann and some of the other observers that this is probably due to a virus, inasmuch as the typical cases all show leukopenia and show no pneumococci or other constant bacterial findings.

It seems to us that we are dealing with a definite clinical entity and the problem of what to call it, I think, can well await the discovery of its etiology.

JOHN T. FARRELL, JR., M.D. (*closing*): The most important thing in the practice of medicine, as far as the patient is concerned, is the diagnosis, but in many conditions, as far as the family is concerned, the most important thing is: what is going to happen to the patient? In a disease like tuberculosis, the economic aspect, the question of insurance, the question of continuing work, the question of marriage, all enter in and we feel that anything which helps to give a more accurate prognosis is of value.

As to the terminology, I would agree that the term "malignant" should be reserved to neoplasm, in spite of the fact that we use the term "malignant hypertension." Possibly it would be better to simplify the terminology and speak of a favorable I, II, III, IV, or an unfavorable I, II, III, IV.

From our own experience we know that bilateral lesions behave differently from unilateral. It might be possible, in a scheme of this kind, to reduce it to the terms of contract bridge bidding, assigning a number for involvement of one lobe; a larger number for the involvement of two lobes, presence of cavitation, caseation, and other numbers depending on the extent and character of the disease so that one would have a numerical basis for the determination of the prognosis.

We have recognized the fact that in a particular instance a single film is often not enough to determine what the prognosis is and we have advocated the use of serial studies.

We realize that there are many other factors—age, race, and the presence of diabetes, which have a good deal to do with prognosis, but we were trying to devise a method which could be applied by the roentgenologist. The value of this report lies in the fact that the prognosis is practically limited to the x-ray findings. If to these one adds the implications of other factors such as age, race, and complications, a prognostic accuracy of more than 80 per cent, which was achieved by the roentgen indications alone, should be possible.

HOWARD P. DOUB, M.D. (*closing*): I wish to say that Dr. Sosman and I are not much at variance in our statements about bronchomycosis. I believe that, in most instances, these mycoses are saprophytes but there are certain cases in which they are primary invaders. In several of our cases, in which we had autopsy confirmation, I believe the mycotic infection was the cause of death.

In coccidioidal granuloma, which occurs mostly in California, it is very definitely a primary infection.

EVALUATION OF ROENTGEN THERAPY IN SINUS DISEASE[1]

By J. R. MAXFIELD, JR.,[2] A.B., M.D., Instructor in Radiology, *and* CHARLES L. MARTIN, E.E., M.D., Professor of Radiology, Baylor Medical College, *Dallas, Texas*

From the Radiological Service of Baylor University Hospital, Dallas, Texas

ALTHOUGH the medical men in ancient times did not have the same conception and understanding of the nasal sinuses that we have to-day, they did make references to conditions which, in the light of our present knowledge, can be interpreted as sinus disease. Since Albright (1) has thoroughly covered the history of sinus disease from antiquity to the present time, it is sufficient to say here that until 1850 our modern knowledge and conception of sinus disease were unborn.

From the period of 1850 until 1900, rapid steps were made in the understanding of the anatomy of the bones of the face and of the paranasal sinuses. In this period the names of Caldwell and Luc (23) came into prominence. Caldwell advised making an opening through the canine fossa and a counter-opening through the inferior meatus. The primary opening was allowed to close and treatment was carried on through the opening in the meatus. In 1903, Luc described a similar approach and advised complete removal of the lining membranes. The accomplishments of these men marked the beginning of radical nasal surgery which reached its height about 1915.

Surgeons and rhinologists of this era from 1850 until 1915 were attempting to relieve the pathology in the accessory sinuses by surgical procedures, that is, by attempting to modify the anatomy of the accessory nasal sinuses. Their byword was drainage, drainage, and more drainage. When their surgical procedures failed, more radical ones were advised in an attempt to turn failure into success by more surgery. The end-results in most instances, however, were most unfavorable. The adage grew, and was true, that sinus surgery—once performed—required sinus surgery from then on.

About 1913 there began a metamorphosis from the radical opinion held by the rhinologists to one of conservatism. Pathology in the accessory sinuses was being studied in an attempt to explain their diseases. The consistent failure of the radical procedures forced the surgeons to turn to physiology and biology for an explanation of "why the surgery failed." The consensus of opinion of the more conservative, better trained men in otolaryngology is expressed by the following quotation from Wright (23):

"The period of my activity, covering as it does more than 25 years, witnessed the absurd exaggeration of notions as to the frequency when sinus disease required surgical intervention and the rash resort to this devastating destruction of nasal structures in operative measures designed to afford relief to affections more or less trifling in themselves. It experienced the disappointment of too enthusiastic operators and too credulous patients. It saw reputations, world-wide in the domain of our specialty, made out of a manual dexterity perhaps, but also an intrepidity of spirit which often approached too much upon the rights of humanity and too often disregarded the precepts of conscientious professional contacts."

By 1915 a better understanding of the function of nasal sinuses in health and disease was being manifest. The action of the cilia in the sinuses was demonstrated to be a protective mechanism. The names of Bloomfield, Yates, Hartz, Hilding, Pretz, and others appeared in the literature. Attempts were made to impress the rhinologists with the importance of the protective mechanism present in all si-

[1] Read before the Texas Radiological Society at the Annual Meeting in San Antonio, Oct. 22, 1938.

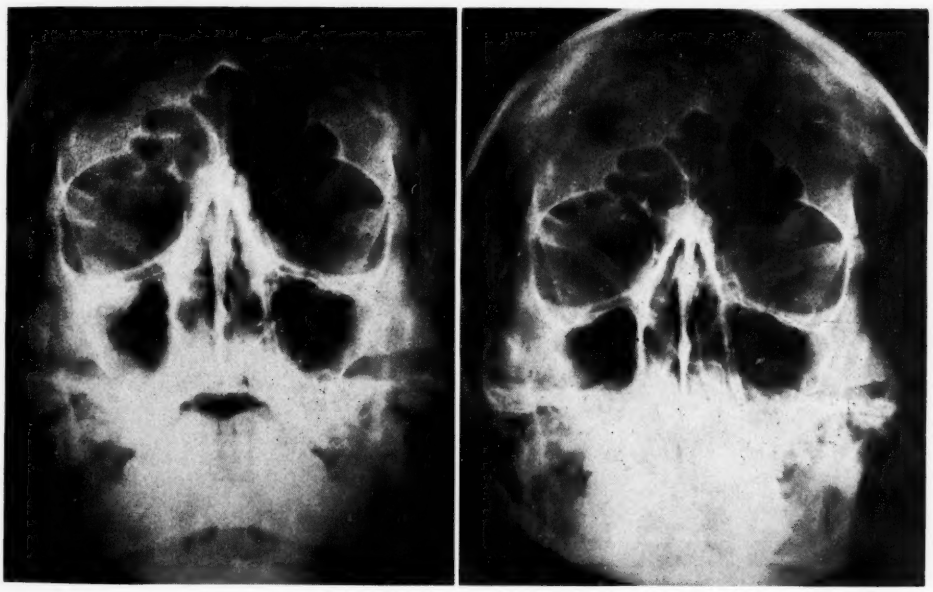
[2] Now Instructor in Roentgenology, University of California Medical School, San Francisco.

nuses. Operators began to realize the importance of the preservation of the normal protective mechanism instead of attempting to correct the defects of Nature in anatomical structures, and thereby hoping to secure drainage by gravity, but the day of radical surgery had not passed. New methods of attack from an anatomical standpoint were reported and countless hundreds of patients were being subjected to radical sinus operations month after month and year after year. This condition is still present in our modern era but, fortunately, a more marked trend toward conservatism is manifest than at any time in previous years.

Even as late as the past decade conflicting reports can be found coming from the same institutions as to the values and results of surgery on the accessory nasal sinuses. Hilding (8), at the Mayo Clinic, reports that the results of operation on the accessory nasal sinuses in general are not entirely satisfactory. With this in mind his series of experiments on the physiology of the nose and sinuses were carried out in the hope of finding possible causes for failure of operations on the sinuses. From this same institution and covering the same general period is the report of Williams (21), in which he says that 200 cases, studied at the Mayo Clinic, operated on in 1926, showed 84.6 per cent cases of symptomatic relief and

TABLE I.—RESULTS REPORTED FROM SURGERY

	Cured	Improved	Unchanged
Barlow	47%	30%	23%
Tucker	99%	1%	0
Stevenson	94%	3%	3%
Williams	84.6%	12.4%	3%
Thorburn and Patozzi	43%	35%	22%
Richards	34%	20%	46%



A *B*

Fig. 1. Miss H. H., white, nurse by occupation, aged 26 years. Symptoms of three months' duration—purulent discharge, severe headaches, morning cough—no relief from conservative treatment.

Fig. 1-*A*. Roentgenograph made Dec. 1, 1937, reveals proliferative soft tissue in lateral portion of right antrum, with increased density in right frontal sinus. X-ray therapy: Dec. 3, 1937, 400 r to sinuses.

Fig. 1-*B*. Roentgenograph made Jan. 3, 1938, shows sinuses clear. Complete symptomatic relief. Remained well for 11 months, then, following an acute cold, developed symptomatology and radiographic findings similar to those found on first visit. Radiation therapy (Nov. 19, 1938) gave relief and the patient has continued well until the present time.

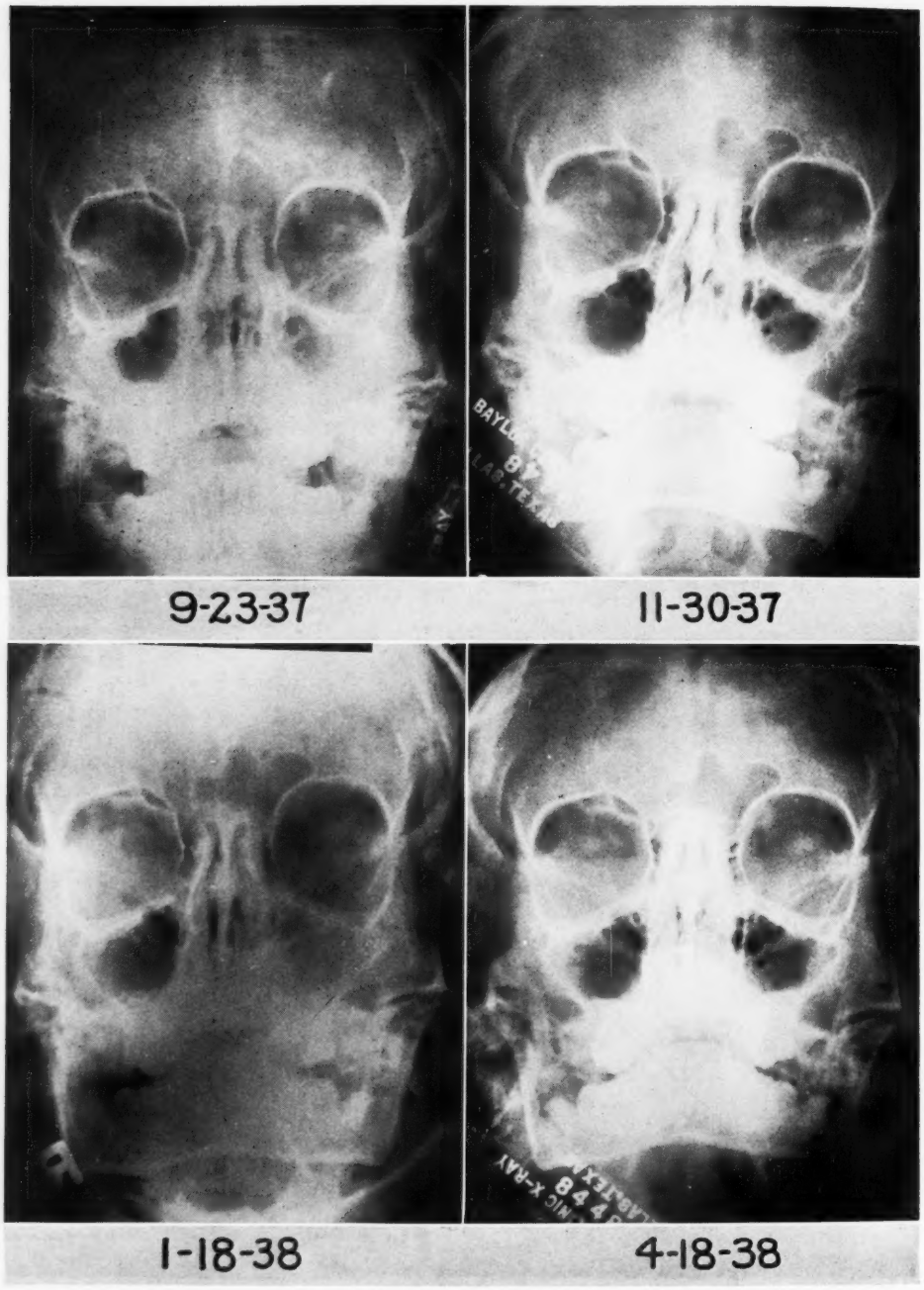


Fig. 2. D. H., white, male, aged 13 years. History of sinus disease for several years. Intensive treatment by allergy department, nasal packs, nose drops, etc., for six months without relief.

Fig. 2-*A*. Roentgenograph made Sept. 23, 1937, shows proliferative soft tissue in both antra. Roentgen therapy (300 r).

Fig. 2-*B*. Roentgenograph made Nov. 30, 1937, shows definite improvement: all symptoms relieved. Jan. 2, 1938, for check-up routine examination; no complaints; doctor prescribed nose drops for dry nasal

only 6 per cent that required a second operation, "the condition having cleared up not only from the patient's standpoint but from our standpoint as well. . . . . These results should tend to change the opinion which is sometimes expressed by the uninformed that it is difficult to secure symptomatic relief in chronic sinus disease, at least insofar as the maxillary sinus is concerned." With two such reports from the same institution, it is little wonder that the general practitioner or the oto-laryngologist in the smaller centers is in a quandary as to which to follow. The results shown in Table I also tend to emphasize the great variation in the results of treatments in various institutions. It does bring one to feel very definitely that the answer to the sinus problem is not yet at hand and that radical surgery is not the answer to the handling of all sinus disease. These few brief quotations will sum up the period to the present time.

Jervey (9), in 1935, said: "Suffice it to say that to-day the trend of radical surgery is on the wane, though we still hear of interns at special hospitals who boast of the number of 'radicals' which they have done without, unfortunately, a check-up on end-results." He stresses that an attenuated sinus cannot be restored to a normally functioning sinus.

Hays (7), in 1937, said: "With the attendance upon thousands of patients with nasal complaints in over 25 years of specialized practice, I believe I am in a position to state that the majority of prospective sinus conditions should not be operated on and that almost without exception the majority of sinus infections will recover if treated conservatively."

Snow (17), in 1937, said: "Sufferers from sinusitis want relief from pain and discomfort . . . granted that surgical intervention is occasionally necessary, operative procedures fall far short of being satisfactory as attested to by patients and internists alike."

Buckley (3) said: "When operation is done, regardless of the kind, the nose is mutilated to a certain degree and unless the result is going to more than compensate for the mutilation, we are not going to do any good but we are actually hurting our patient."

Salinger (14), in 1937, said: "The literature in 1936 reveals nothing revolutionary or startling. It is nevertheless significant in demonstrating a saner appreciation of basic anatomic and physiological data and manifesting a more conservative medical and surgical treatment."

The surgery of the accessory nasal sinuses has not been entirely satisfactory; so likewise have failures accompanied other methods of treatment that have been introduced. The main point in favor of some of the conservative methods of treatment over surgery is that they do not damage the patient as much. It is universally accepted that poor medical results can quite easily be supplemented by surgical procedures, but poor surgical results cannot easily be corrected by medical treatment.

We do not mean to leave the impression that we condemn all surgery of the accessory nasal sinuses. It is obvious that when the normal ostium is completely blocked, surgery is indicated. Patients with symptoms such as pain, headaches, etc., with a rise in temperature, and a swelling of the surrounding tissue, require immediate operation. If operation is unduly delayed in such a case, not only is there a risk of serious complications arising from the extension of the inflammatory process but ultimate healing may be definitely postponed.

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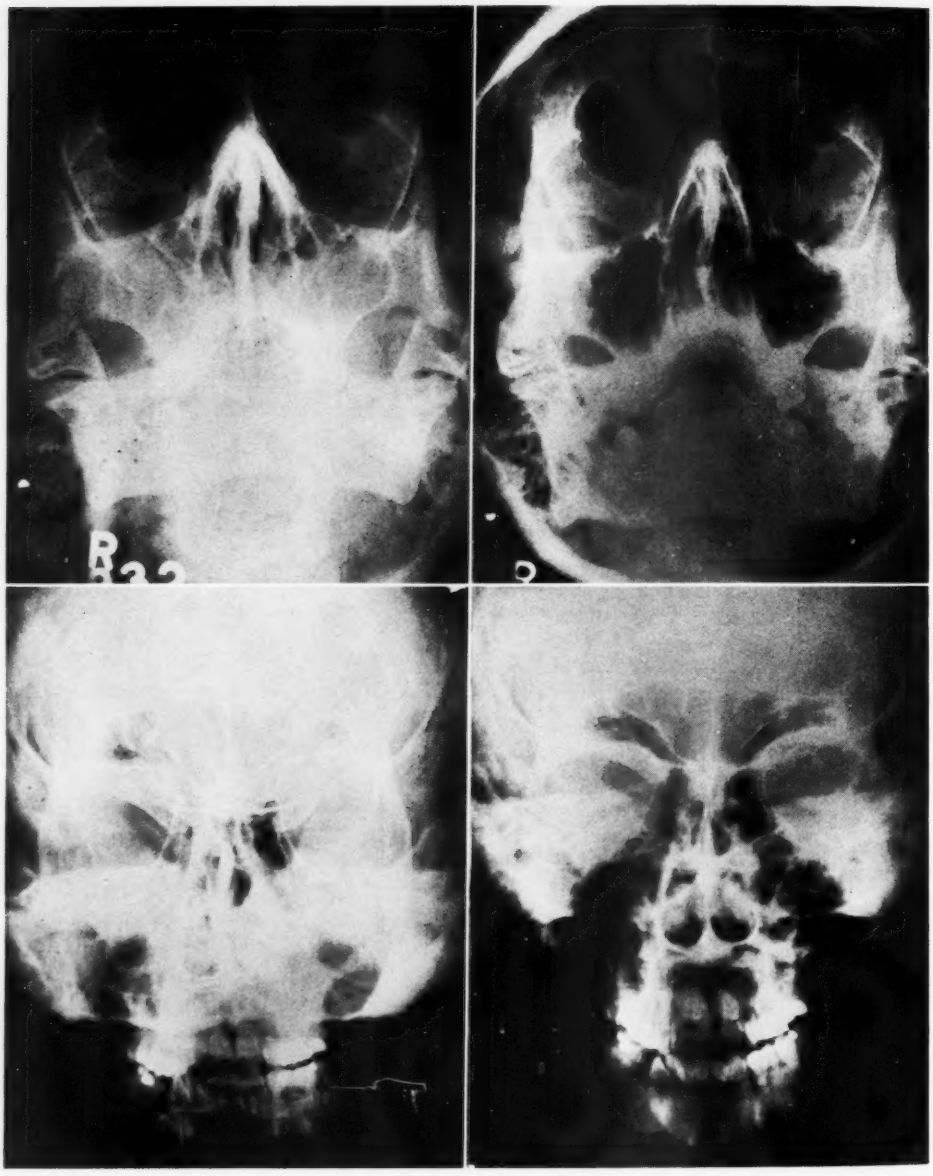
mucosa; symptoms reappeared and in ten days there was copious purulent discharge from antra, and severe headaches. Nose drops were discontinued; no relief.

Fig. 2-*C*. Roentgenograph made Jan. 18, 1938, shows increased density in left maxillary antrum. X-ray therapy (300 r).

Fig. 2-*D*. Roentgenograph made April 18, 1938, shows normal radiance of sinuses. Patient began to improve 48 hours after treatment and completely recovered. In response to a questionnaire, he reports that he has remained well since the last treatment.

Perhaps one of the reasons that diseases of the sinuses have been such a problem is that the sinuses, in addition to being a seat of infection themselves, can also be a deli-



A *B*

Fig. 3. Mrs. L. W. M., white, aged 31 years, had sinus trouble "for years." Breathes through her mouth at night, expectorating large amounts of muco-purulent material on arising. Complained of cough, and pain over the antra. Roentgenograph "A" (Dec. 1, 1937) shows increased density of marked degree in both maxillary antra, with right ethmoid cloudy. After x-ray therapy (400 r), patient's headaches were completely relieved; cough and expectoration markedly diminished. Roentgenograph "B" (Jan. 3, 1938) shows all sinuses clear. In response to a questionnaire, patient reports she is now symptom-free for first time in many months.

cate register for changes in other portions of the body of a physiological and pathological nature, as pointed out by Oaks, Merrill, and Oaks (10). Many pathological conditions in the body first show their recognizable symptoms in the membranes of the nose and sinuses.

Many plans of treatment have been devised in an attempt to find a specific therapeutic plan for treating sinus disease, but the horizon has been clouded by failures to the present time. It is true that a few patients will respond to this plan of treatment or that plan of therapy, but who knows but what the patient would have gotten spontaneous relief if left alone. Wenner (20) suggested the use of suprarenal cortex and reported experiments carried out in rabbits with infected sinuses, in which suprarenal cortex was used with good results. But the use of this type of treatment on patients with sinus disease has failed to produce the brilliant results found in experimental animals. Turner and Loew (18) report the use of vitamin A as a method of protection from bacterial invasion of the respiratory tract of rats and suggest vitamin A deficiency as a contributing cause to sinus disease. It is significant that with the widespread use of high vitamin diets and fortification of these diets by synthetic and concentrated vitamin products, if sinus disease is caused by vitamin deficiency, better and more constant results are not obtained. Davison (5) believes this is also true in the allergic type of therapy since the results obtained in treating sinus disease on the basis of allergy are not encouraging except in very carefully selected cases. Reisman (13) believes that when allergy is present it is probably the result of the patient's being sensitized to the proteins in the exudate formed in his own sinuses. If this is true, attention should be focussed upon the sinuses themselves, which are the causative factor, rather than upon the resulting allergy.

The otolaryngologist can relieve a large proportion of the acute or subacute types of sinusitis and a goodly number of the so-called chronic cases, with the use of sound conservative therapeutic procedures. The radiologist enters the picture when, after several treatments, the patient is showing no response.

Radiation therapy can at best relieve only the pathology present in the sinuses. It cannot keep the factors which produce the original disease from causing sinus disease a second or a third time as so frequently happens. Several of our cases have had a recurrence of symptoms, months after treatment. The patients who got relief from the initial treatment also were relieved by subsequent treatments (Figs. 1 and 2).

Osmond (11), in 1923, wrote the first article referring to therapy of the paranasal sinuses by roentgen rays, describing the treatment of acute infections of the antra and frontal sinuses with good results. He stressed that he had not found a method of treatment for all sinus disease.

Butler and Woolley, (4), Warren (19), Smith and Nickel (15), Bernheimer and Cutler (2), and others agree that the greatest benefit to be obtained from radiation therapy of the sinuses is in the hyperplastic type of sinusitis in which radiographs show thickened membranes and the patients usually have a thin watery discharge and give a history of colds or chronic cough. The shorter the duration of symptoms, the better the chance of good results, and the greater the possibility of a permanent cure. This coincides completely with our impression of the problem in that our best results have been obtained in cases of this type (Table II).

Since some cases of the chronic type of sinusitis are known to get seemingly miraculous symptomatic relief from radiation therapy, it is of value to give one series of treatments in an attempt to evaluate the response of the individual patient. Several of our patients with chronic changes in the sinuses got prompt relief of all disturbing symptomatology following radiation therapy (Fig. 3).

Fenton and Larsell (6) believe that the benefit of x-ray therapy is due to the early

destruction of lymphocytes in the infected membrane, with an increase in the number of macrophages and an increase in histocytes. These writers state that, after a week or more, some fibrosis begins to appear, but they do not stress this point. Larsell has stated that, with x-ray therapy in the doses given, there is no evidence of destruction of ciliary epithelium or other cellular elements other than lymphocytes.

This fibrosis, in our opinion, is the most important part of the effect of radiation therapy, and this probably accounts for the good results obtained in the hyperplastic type of thickened membrane, relatively recent in its formation. We feel that there is a definite relationship between the responses of these thickened hyperplastic membranes and the responses obtained from the treatment of keloids by radiation therapy. We know that if a keloid has been present over a period of years, usually little or no response can be hoped for by radiation therapy, while keloids resulting from burns, cuts, etc., of recent occurrence will respond nicely to radiation therapy, and that radiation therapy following surgical removal of keloids will prevent recurrences.

The connection, therefore, seems to be that sinus pathology which has been present over a period of years has undergone the same type of change that the keloid has undergone and has become resistant to radiation therapy, while the thickened membranes of shorter duration are affected by radiation therapy. Little can be done by x-ray therapy, except in some few instances, to alleviate the symptoms in cases in which the antra are completely filled with hyperplastic tissue of long duration, but, following radical surgical operations on the antra, sufficient x-ray therapy, if given immediately, will, in most cases, prevent a return of the hyperplastic tissue in the antra, as so frequently occurs.

We advise radiation therapy in sinus disease only after a thorough treatment of the patient with conservative measures by a competent otolaryngologist. We have a definite feeling that, since some patients obtain such brilliant results from roentgen therapy, it should be used on all cases before extensive operative procedures are done, except when the patient's condition demands immediate operation. The patient should be informed of the uncertainty of good results but should also be assured that the treatment is easily given and carries with it little morbidity in the hands of a capable radiologist. Following any operative procedure on the sinuses, radiation therapy should be given as above advocated.

Radiation therapy is definitely contra-indicated when there is not good drainage through the natural ostium or through "windows" in the sinuses. It is also contra-indicated when there is a tumor mass in the sinuses, since malignancy must then be suspected and biopsy be done for microscopic diagnosis. These are the only two definite contra-indications that we

TABLE II.—RESULTS ACCORDING TO TYPE OF PATHOLOGY

	No. Cases	Cured	Improved	Unchanged
Acute Uncomplicated	16	7	8	1
Acute Complicated	9	1	2	5
Chronic Uncomplicated	18	2	6	9
Chronic Complicated	14	0	2	12

Acute Uncomplicated: Rapid onset; short duration with symptoms of pain, drainage, headaches, etc. Edema and proliferation of muco-periostium blurs sinus outline.

Acute Complicated: Case with the above symptomatology plus acute iritis, conjunctivitis, abscess formation, etc. Blurred sinus outline plus increased density throughout.

Chronic Uncomplicated: Sinus disease of over three months' duration with or without pain, drainage, headaches, etc. Thickened membrane and condensing osteitis present.

Chronic Complicated: Case with above symptomatology plus bronchiectasis, asthma, rheumatism, polyps, etc. Findings same as above plus possible soft-tissue shadow in sinus.

TABLE III.—RESULTS IN NINE CASES WHICH HAD BOTH PROLIFERATIVE MEMBRANES AND POLYPS OR MUCOCELE

	Cured	Improved	Unchanged
Proliferative membranes	3	5	1
Polyps or mucocele			9

have encountered. Table III shows the results that were obtained in the treatment of nine cases with both tumor masses and hyperplastic membranes in the antra. Following radiation therapy, operative removal was done on seven of these cases, six with polyps and one with a mucocele. Two of the patients refused operation since they were already comfortably relieved of their symptoms. We do not advise treatment of cases with definite soft-tissue masses in the sinuses, and have stopped doing it ourselves until after operative removal of the mass.

TABLE IV.—RESULTS BASED ON DOSAGE

(All cases followed for six months or longer)

	No. Cases	Cured	Improved	Unchanged
Heavy dose, 400 r or more	43	10	16	17
Light dose, 300 r or less	14	0	4	10

(r unit measured in air)

We insist upon having our cases followed carefully by an otolaryngologist who stands ready to assist us at all times. This has acted as a balance for our early enthusiasm of radiation therapy in sinus disease and has helped us to arrive at a critical evaluation of the merits of the procedure. Although the percentage of cured (I believe we would do better to use the word "relieved") cases is about 18 per cent, there is a definite use for radiation therapy in handling diseases of the nasal sinuses.

It is encouraging to see the marked relief some of the patients receive. One patient was referred to us by the otolaryngologist after she had been to the departments of medicine, allergy, endocrinology, and chest. She had as her main complaints, cough and a slight sore throat, with some headache, for about a year before admission to the radiology department. For eight months she had had intermittent attacks of asthma at intervals not exceeding a week apart, which had grown much more frequent for the past few weeks in spite of allergy and endocrine therapy. Roentgenographs (Fig. 4-*A*) showed marked proliferation of the membranes in both antra, particularly on the right, and increased density in the right frontal sinus. Following radiation therapy she has not had another attack of asthma up to the time of this report, 20 months since therapy was given. She has gained 23 pounds and her sinuses appear clear in the roentgenographs as shown in Figure 4-*B*. All of our cases have not resulted in such dramatic relief by any means. However, when such relief does occur, even in a small percentage of cases, it is certainly worth while to give radiation therapy to those cases not relieved by other methods of treatment, particularly when radiation therapy is so easily administered by the radiologist and so well tolerated by the patient.

TABLE V.—CASES ACCORDING TO PREVIOUS TREATMENT

	No. Cases	Results of Previous Therapy			Results of X-ray Therapy		
		C	*I*	*U*	*C*	*I*	*U*
Medical	24	0	8	16	7	6	11
Conservative surg.	17	0	2	15	2	5	10
Radical surg.	8	0	0	8	0	2	6
Allergic	3	0	1	2	1	2	0
Diathermy and short wave	4	0	1	3	0	4	0
Vaccine	1	0	0	1	0	1	0

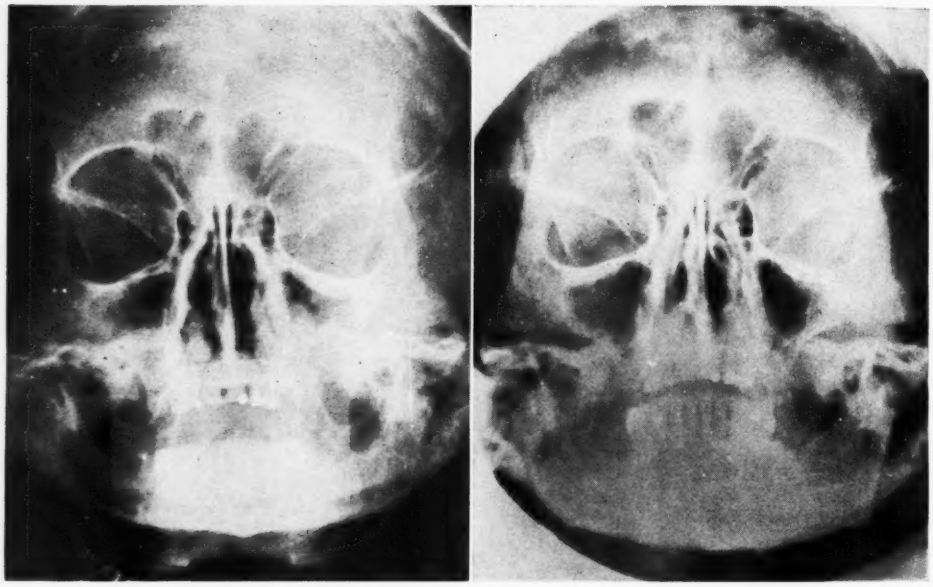
C = Cured.
I = Improved.
U = Unchanged.

Table V shows the comparison of results obtained by radiation therapy with the result obtained in the same case by another method of treatment. In reviewing the table, it must be remembered that these patients were having a return or continuance of their symptoms; also that the cases cured by the other methods of therapy were not shown because these cases were never seen by the radiology department.

Insofar as the actual treatment of the patient with radiation therapy, methods of technic are easily available. As has been stressed time and time again, not only in

connection with this type of therapy but in connection with all radiation therapy, it should be carried out only by a thoroughly competent radiologist who realizes the power of the agents which he uses and the posterior, to cross-fire the posterior cells of the ethmoids.

Our present technic closely parallels this, being 200 kv.p., 25 ma., 50 cm. distance, 0.5 mm. copper and 1 mm. aluminum for 10



A *B*

Fig. 4. Mrs. J. R., white, aged 61 years. Asthma, dizziness, and post-nasal drip for one year. Treatment by allergy department, conservative medical and surgical methods, with no relief.

Fig. 4-*A* shows soft-tissue proliferation with blurring of sinus outlines in both antra, particularly the left. X-ray therapy given.

Fig. 4-*B*, made two months later, shows marked improvement in appearance of sinuses. Patient much improved; no asthma since therapy (20 months). Patient gained weight for first time in several years.

terrible effects which can result from their improper use. Irreparable damage and untold suffering can result from the unskillful and careless application of treatment.

Dr. Woolley (22) has given me his latest technic which is not yet published and which is as follows: 200 kv.p., 20 ma., 55 cm. distance, 0.25 mm. copper and 3 mm. aluminum filter, for 10 minutes, which gives approximately 530 r, with back-scattering, through two ports. Port I is an oblique one, through the right side of the face, using a lead mask which exposes only the right maxillary, ethmoid, and frontal area. Port II is the same on the left side. The central rays are directed obliquely minutes, which gives us 400 r, measured in air, without back-scatter, through the single port. The eyes and eyebrows are covered by a lead shield and a lead rubber mask is put over the hair line and just above the chin so that only a 15 × 15 square over the region of the frontal, maxillary, and ethmoid sinuses is exposed.

Smith and Nickel feel that moderate dosage should be used rather than heavy dosage. Rathbone (12) feels that the quality of the radiation is probably of no significance so long as some filtration is used. Rathbone and Smith and Nickel give fractional dosage at intervals for a total of some three to eight treatments. Butler

and Woolley feel that a single full dose gives better results than fractional doses given at intervals. We have used both light dosage and heavy dosage (Table IV). Our experience verifies the findings of Butler and Woolley—that the full single dose gives better results than multiple fractional doses. We now use only the heavy dose method of treatment.

TABLE VI.—RESULTS REPORTED FROM X-RAY THERAPY

Stevens	Cured 80–90%	Improved Not available	Unchanged
Smith and Nickel	60%	78%	12%
Rathbone	57%	28%	15%
Bernheimer	52%	38%	18%
Butler and Woolley	31%	50%	19%
Warren	25%	60%	15%
Martin and Maxfield	18%	35%	47%

Following treatment, our patients have complained of feeling a fullness of the face and increased discharge for from 24 to 72 hours. Following this period, there is a decrease in the amount of the discharge, with a thickening of the discharge itself. If pain is present, it is usually relieved in 72 hours. The patients getting relief during the first 24 to 48 hours following the treatment usually get the best results. The maximum response is usually reached in three to four weeks following therapy. We have found that in most of the cases in which relief has been obtained, a single treatment has sufficed. In cases in which relief has been gained from a single treatment, we have had no hesitancy in repeating the treatment if the symptoms returned and if there had been a sufficient interval of time since our previous treatment. We do not feel justified in continuing the treatment of patients who have received no symptomatic or roentgenographic evidence of relief. Although a few of our cases have been spectacular in the results obtained, unfortunately our percentages of relief and permanent cure are small. We have not been able to confirm the results reported elsewhere. The tabulation of our results are shown in Table VI.

CONCLUSIONS

We feel that although radiation therapy does give relief in a certain percentage of cases, it is not a panacea for all sinus diseases; that it should be used only after conservative therapeutic measures have failed; that it should be used before radical surgery, since it does occasionally produce phenomenal results; that it should be used following all surgery on the sinuses, and that it should be carried out not in competition with but in co-operation with the otolaryngologist and the referring physician.

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PULMONARY INVOLVEMENT IN THE LYMPHOBLASTOMAS: SPECIAL REFERENCE TO ROENTGEN ASPECTS[1]

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THE relative scarcity of articles in the current literature upon pulmonary involvement in connection with the lymphoblastomas would seem to justify the reporting of a series of such cases which the writer has observed within the last few years.

The term "lymphoblastoma" has been used to include a large variety of conditions involving the lymphatic and hematopoietic systems by different authors, Peirce, Jacox, and Hildreth (1) having tabulated 17 separate entities under it. For the purposes of this paper, Hodgkin's disease, lymphosarcoma, and chronic lymphatic leukemia only will be given consideration. The roentgen findings in these conditions are sufficiently alike to warrant grouping them as a unit. Although mediastinal, hilar, and pleuritic lesions are commonly associated with parenchymal involvement, cases in which these structures only appeared to be involved are excluded from this discussion.

As regards incidence, statistics would indicate a rather high percentage of lung involvement. In instances in which these are based on autopsy records, this does not seem surprising inasmuch as the terminal stages of these diseases are undoubtedly associated with more or less generalized dissemination by metastasis or secondary invasion. Many of the changes noted at the postmortem examination are not demonstrable clinically or roentgenologically, which may explain the common impression that such involvement is rare. The high incidence reported by some authors from studies of the living is probably due to the inclusion of lesions limited to the mediastinal and hilar lymph nodes which are relatively common. Falconer and Leonard (2) cite percentages in Hodgkin's disease ranging from 28 to 61 obtained from 125 cases, including 20 of their own, reported by various authors, giving an average of 37.6 per cent. Kirklin and Hefke (3) have reported a 30 per cent incidence in Hodgkin's disease, 23 per cent in lymphosarcoma and six cases of chronic lymphatic leukemia in 48 cases of leukemia. Falconer and Leonard (4) found 36 per cent involvement in 25 cases of lymphosarcoma, and 30 per cent in 30 cases of lymphatic leukemia which they observed. Versi (5) gives a 40 per cent incidence and Moolten (6) states that of 18 most recently autopsied cases in the Mount Sinai Hospital, pulmonary lesions were present in nine and in two others lesions existed within the mucosa of the trachea and bronchi.

The 35 cases which form the basis of this paper, consisting of 24 cases of Hodgkin's disease, six of lymphosarcoma, and five of chronic lymphatic leukemia, are not available for reliable statistics. They constitute about half of all of the cases referred to the author's department for diagnosis or treatment, and they have been diagnosed roentgenologically as probable intrathoracic lymphoblastomas, including mediastinal and hilar involvement. During the same period of observation, our hospital records showed positive biopsy reports of 130 cases. Assuming that all of these cases had roentgen examinations of the chest, it would appear that slightly less than 50 per cent had intrathoracic involvement and in at least 25 per cent pulmonary involvement was present. In 33 of the 35 cases used in this study, the presence of lymphoblastomas was confirmed clinically by biopsy and other examinations; in the other two irradiation

[1] Presented before the Twenty-fourth Annual Meeting of the Radiological Society of North America, at Pittsburgh, Nov. 28–Dec. 2, 1938.

response and other factors left little doubt as to the probable nature of the condition. The lymphoblastomatous nature of the lung changes in most of the cases would seem to have been proved by the fact that they regressed in whole or part after irradiation, as will be discussed briefly in connection with therapy.

Accurate estimates of incidence in the living can be made only if all cases be subjected to roentgen investigation, for this is usually the only certain means of determining pulmonary involvement. This fact has been impressed upon us rather forcefully since we have routinely examined chests roentgenologically in all cases referred to us for irradiation therapy of superficial nodes of lymphoblastomatous origin. Intrapulmonary or other intrathoracic involvement has repeatedly been noted in cases in which there were few or no signs or symptoms suggesting such involvement and no chest examination had been requested.

The pathologic changes found in pulmonary lesions in Hodgkin's disease have been studied in detail and reported by Moolten, and since these changes suggest what the roentgen examination may disclose, it might be well to describe them at length. According to Moolten, the bronchi are conspicuously involved and the entire substance of the walls forms a matrix for the evolution of granulomatous changes. The granuloma is not limited by fibrous tissue sheaths but spreads into the alveolar parenchyma in the manner of a peribronchitis or peribronchial pneumonia. Combinations of granulomatous bronchitis, peribronchitis, lymphadenitis, and perilymphadenitis may produce obliteration of considerable parts of the lung parenchyma, especially around the hilum. There may also be pleurogenous spread which may increase the magnitude of involvement. The process is not confined to lymphoid tissue but may implicate mesenchymatous elements. The granuloma may undergo fibroblastic transformation and in the late stages dense cicatrization may occur. Extensive areas of lung parenchyma may be transformed into solid areas by granulomatous invasion of interstitial tissue between alveoli and the obliteration of them. The bronchial lumen may be affected both as regards its caliber and lining. Polypoid growths may occur in the bronchus and obliterate its lumen, resulting occasionally in atelectasis and bronchiectasis. Abscess formation also has been described. So-called Hodgkin's sarcoma or reticulum-cell lymphosarcoma may be a proliferative phase of the disease.

Part of the parenchymatous changes in the lungs in Hodgkin's disease may be nonspecific, *i.e.*, they may be in the nature of a catarrhal alveolitis or mild irritative pneumonia due to the virus or toxin of the disease rather than to granuloma. There may be an exudative phase with changes general to acute or subacute inflammation.

Search of the available literature has failed to reveal similarly adequate descriptions of the lung pathology associated with lymphosarcoma or chronic lymphatic leukemia. Moolten, in a comparative paragraph, states: "In cases of lymphosarcomatosis involving the lungs, bulky infiltrated alveolar septa may be seen resembling in some respects the analogous condition in Hodgkin's disease." In one of our cases of chronic lymphatic leukemia with pulmonary involvement, the autopsy protocol stated that there were poorly defined nodular areas in both lungs and microscopically there was increase of interstitial tissue in focal areas with dense collections of lymphoid cells. The similarity of roentgen findings encountered in all three conditions would indicate that whatever minute variations occur, the gross pathologic changes resemble each other very closely.

In trying to translate the pathologic changes occurring in the lungs in lymphoblastomas into terms of roentgen images, one is confronted with the usual difficulties encountered in most chronic or slowly developing pulmonary lesions. Site of origin of the disease, stage of development, predominating characteristics of the pathologic changes, and possible com-

plications will all influence the picture presented. A classification for the lesions of Hodgkin's disease suggested by Versi, based on anatomic and roentgenologic features, would seem to serve as an excellent basis for interpretation.

1. Mediastino-bronchial node formation with direct invasion of lung tissue.
   (*a*) By the hilum.
   (*b*) By the medial surface of the lung.
2. Mediastino-bronchial node formation and peribronchial and intrabronchial spread in the lungs.
3. More or less lobar (diffuse) lung infiltration with varying degrees of involvement of the bronchomediastinal lymph nodes.
4. Confluent lobular (isolated circumscribed) focal formation in the lungs with involvement of lymph nodes as above.
5. Miliary dissemination (lymphohematogenous) with involvement of lymph nodes as above (1).

To this might be added occasional atelectasis, bronchiectasis, abscess formation, and a fairly common accompanying fluid accumulation in the pleural cavities as complicating factors.

In going over our cases, we find that all of them conform to one or the other of the above types. Interpretation is comparatively easy if a generalized adenopathy or other signs of lymphoblastoma are present. In the absence of these, in instances in which the patient is first examined because of pulmonary symptoms, the roentgen differentiation may be extremely difficult or even impossible. After other causes have been eliminated as far as possible, an intensive search may reveal inconspicuous enlarged lymph nodes available for biopsy confirmation, or test irradiation may reveal the nature of the condition. Realization of the possibilities of lymphoblastomatous involvements in the lungs and familiarity with the findings they present are prime factors in their recognition. An observation credited to Bernard, and quoted by numerous authors to the effect that a fluid accumulation in the pleural cavity, of unknown origin should suggest the possibility of lymphoblastoma, deserves consideration.

As regards the symptomatology which may be directly ascribed to the pulmonary involvement in the lymphoblastomas, a non-productive cough, dyspnea, and occasionally chest pain or feeling of oppression are common findings and were present in over half of our cases. Other signs of the disease—such as a generalized adenopathy—were present in the great majority of cases and about half of the patients complained of malaise, weakness, or loss of weight. In three instances there was a pronounced pruritus, two patients had specific skin lesions, four gave a history of fever, and nine had fluid in the pleural cavity. No definite conclusions could be drawn of the time the pulmonary involvement bore to the course of the disease, but in several of the cases which were followed from the early stages it occurred as a late or terminal condition. As to age incidence, the youngest patient of the series was nine and the oldest 61, with an average of 35.5 years for the entire group. The Hodgkin's cases averaged 32 years as compared to 42 and 43.5 years for the lymphosarcomas and lymphatic leukemias, respectively. Males and females showed an equal ratio in the Hodgkin's group but there were five males to one female in the lymphosarcoma cases and four to one in the lymphatic leukemias.

In the accurate diagnosis of pulmonary lesions of lymphoblastomatous origin, biopsy findings form the most reliable criteria although regression with irradiation is, in most instances, almost equally conclusive of such involvement. Tumorous masses in the mediastinum, with or without enlarged hilar nodes, and pulmonary infiltrations usually in close proximity to them, are strong presumptive evidence that the condition is of this nature, especially so if the changes are bilateral. Differential diagnosis among the three divisions of this group of diseases is generally admitted to be impossible from the roentgen standpoint, and, although some authors have called attention to individual

variations in the appearance of the lesions or response to irradiation, these variations do not occur with sufficient frequency to render them generally applicable. Kirklin and Hefke have reviewed the conclusions of numerous observers in this respect at some length. The possibility of associated lesions must always be borne in mind, for which reason mediastinal enlargements in suspected cases must be carefully analyzed as possibly being due to substernal goiter, thymoma, paravertebral abscess, or aneurysm. Pulmonary cancers, either primary or metastatic, may on occasion give almost identical pictures and in the absence of other identifying data, test irradiation may be of utmost value. Rarely, pneumoconiosis or chronic pneumonitis may present confusing pictures but usually the history or clinical data permit of easy differentiation. Pulmonary tuberculosis occasionally offers difficulty in differential diagnosis especially in cases in which definite evidences of lymphoblastoma are present and in which the lungs show calcification or other residual changes commonly considered characteristic of tuberculous origin. Lack of response to test irradiation may be of great value in determining the nature of the pathology.

Just as it is almost impossible to correlate the time of appearance of pulmonary involvement with the course of these diseases, so, too, their recognition offers no reliable prognostic indication of the subsequent duration of the disease. Some of our cases were followed for several years after the diagnosis was made (one of them for over five years) and others terminated shortly after its recognition.

As regards the irradiation treatment of pulmonary lesions of lymphoblastomatous origin, it has been stated that these lesions are more radioresistant than superficial nodes; this has not been our experience. Of the 26 cases of our series which had roentgen therapy, 16 showed well marked regression which was repeated in several of them after recurrences. Three of them showed only partial regression. One of these had no biopsy but had generalized adenopathy which responded well to irradiation. (She was observed over nine years, five years intervening between recognition of pulmonary involvement and fatal termination with pleuritic complications.) One other of these three had questionable pathologic findings after two biopsies. Four of the patients showed practically no change, and in two of these the roentgen findings, although consistent with Hodgkin's disease which according to biopsy report was present, showed calcification suggestive of an old tuberculous lesion. One of these four, whose biopsy diagnosis was lymphatic leukemia, had an interstitial fibrosis which may have been the result of an industrial hazard. The fourth case, also one of Hodgkin's disease, had bone lesions as primary manifestations and ran a rather rapid course. Two cases in the Hodgkin's group showed progressive changes; one of these also had marked bone changes and succumbed shortly after he first came under observation. The other was diagnosed as Hodgkin's sarcoma. One other case included in this series has been similarly classified but roentgen therapy given him has been of too recent date to permit of drawing conclusions as to results. Four of the six cases of lymphosarcoma received irradiation and all of them showed regression. Of the five cases diagnosed as chronic lymphatic leukemia, three received roentgen therapy but only one showed well defined regression of the pulmonary lesion.

A study of the series of cases which forms the basis of this report has led to the following conclusions:

1. Pulmonary involvement of lymphoblastomatous origin is relatively common.
2. Roentgen findings produced by it are sufficiently characteristic to be suggestive of the condition.
3. Routine chest examination of patients known to have lesions apparently limited to the superficial nodes would result in its more frequent recognition.
4. Test irradiation of suspicious lesions is a valuable aid in the differential diagnosis.

I want to acknowledge my appreciation and thanks to Dr. T. J. Wachowski and Dr. J. W. Grossman, of the Department of Roentgenology, for their aid in collecting and preparing the material used in this paper.

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DISCUSSION

GEORGE W. GRIER, M.D. (Pittsburgh, Pa.): I am sorry that Dr. Hartung did not have time to read all of his paper. If he had, I am sure he would have impressed you all, as he did me, by the thoroughness and care with which he has gone into this subject. It is a fine example of what we all should do in studying our cases.

In my own mind I would be inclined to separate lymphosarcoma from leukemia and Hodgkin's disease because I am always expecting to find metastasis or involvement in the lung in lymphosarcoma, but I must admit that I had not been so prone to consider the probabilities of infiltration of the lung in the other two conditions and I was rather surprised to read his figures regarding the incidence of this condition or this complication.

I had been inclined to look on the invasion of the lung, especially in Hodgkin's disease, as a very, very late involvement and to be seen only in the terminal stages. I have been forcefully impressed, by this paper of Dr. Hartung, with the desirability of studying our cases more thoroughly. When we get a cancer of the breast to treat, the first thing we do is to make a film of the chest, and it is obvious to me, after hearing Dr. Hartung, that that is the first thing we ought to do in these cases of Hodgkin's disease and leukemia.

The thing that has impressed me most in this presentation is the high incidence of involvement into the lung; I was particularly glad to hear this paper because the essayist gave proof of the nature of these involvements as examined at autopsy. I have speculated many times as to these involvements, particularly that of Hodgkin's disease—whether they were actually invasions of the lung with what we might call "Hodgkin's tissue," whether they were simply involvement of the lymphoid material in the lung, or perhaps simply cases of atelectasis. Dr. Hartung has analyzed these in his paper and mentions that all these conditions exist. I was glad to learn that the pathologists have found there is definite invasion of the lung by granulomatous tissue—that has cleared the matter up in my mind.

I must admit that I, and possibly others, have been inclined to pass over this question of invasion into the lung as not having much significance, but, as a matter of fact, we can easily see that it does have significance, because these involvements will need treatment just as well as the glands. I am referring entirely to the invasions into the lung and not to the glands in the mediastinum or in the hilus. Of course we all expect them. In Dr. Hartung's paper he mentioned that it was generally considered that these lesions were quite radioresistant, but I believe in his talk here he said that he considered them of the same sensitivity to radiation as the superficial lesion. I am inclined to that opinion.

STEWART HARRISON, M.D. (London): The illuminating paper of Dr. Hartung and the discussion by Dr. Grier on this important subject of mediastinal tumors prompt me to report an experiment that I made some four years ago in Zürich under Professor Schinz and have confirmed recently.

It fell to my lot to collect the material on mediastinal tumors in the Canton Hospital during the twenty preceding years and after excluding, as far as was clinically possible, the type of Hodgkin's disease, the tuberculous type, the thymomas, there remained some 36 cases that fell in the category of tumors of the lymphoblastomatous series.

These tumors were accompanied by the usual clinical symptoms, of course, of a mediastinal tumor, and to a varying degree with blood changes indicating lymphatic leukemia. The blood changes ranged from a maximum of a frank, serious leukemia through the leukemic phases in which the type of lymphocytes present was indicative of leukemia but there was no increase in their number, to cases in which there was absolutely no alteration of the blood picture of any kind.

The point I wish to make is that there were six of this latter kind—tumors of the mediastinum with dyspnea, maybe cough, and no blood changes of any kind, no evidence of Hodgkin's disease, no relapsing temperatures (and they were called lymphosarcoma)—from that, by very small gradations, to the frank lymphatic leukemia tumors.

All of these patients, except two or three who were too moribund, were subjected to radiation of their mediastinal tumors. All with a fairly marked lymphatic leukemia improved, only to relapse, and are now dead following the course of lymphatic leukemia, only too familiar to us all.

Of the six cases in which there were no blood changes of any kind and which were referred to as "lymphosarcoma"—whether or not that is a distinct entity I was unable to conclude—three showed no response at all. They rapidly went downhill and within a month or so were dead.

Of the others, three cleared up, have never relapsed, and remain clear at the present time. The only three in this group of 36 that have cleared up were cases in which there were no blood changes at all and in which the diagnosis was put down without biopsy (which was unobtainable) as lymphosarcoma. I would be glad to hear from Dr. Hartung as to whether or not he has made any such experiments—that tumors of the mediastinum unaccompanied by blood changes give the most favorable distant results after irradiation of a fairly heavy character.

ADOLPH HARTUNG, M.D. (*closing*): I have little to add to my paper. I want to thank Dr. Grier for his kind discussion.

In regard to the remarks of the last speaker, as far as prognosis is concerned, of course the prognosis in practically all cases of lymphoblastoma is bad. Some of the cases that we have observed, as shown here to-day, have been followed for as long a period as nine years and in one of them, in which pulmonary pathology was present, the patient survived for five years after the involvement was noted.

I can give no figures in regard to the blood findings in the cases of lymphatic leukemia, but the last case shown certainly showed no regression under irradiation and most of the other cases that we treated responded in the same way.

YEAST GROWTH: A POSSIBLE TEST ORGANISM FOR X-RADIATION[1]

By OSCAR W. RICHARDS, PH.D., *Buffalo, New York*

From the Research Department of the Spencer Lens Company and the Osborn Zoölogical Laboratory, Yale University

LARGE numbers of yeast may be grown under closely reproducible conditions with little special equipment, because of the accumulated knowledge about the growth of this organism. Even though yeasts were known to be resistant to the effects of x-radiation, the other advantages of this organism suggested that it might be useful as another dosimeter. Preliminary experiments during the Summer of 1931, at the Marine Biological Laboratory, showed that the population growth was arrested for a time by x-radiation, then the culture apparently recovered and continued to grow at the original rate. The period of arrested growth varied with the amount of radiation.

I

The resistance of yeast to x-radiation may account for a considerable part of the lack of agreement in the published investigations. In some of the publications on this subject it is not clear which species of yeast was used or that the cells were grown under optimum conditions. Fresh baker's yeast was found to be little affected by x-radiation (Wels, 1924). Nadson and Zolkevic (1923) showed that potassium chloride had a protective effect when yeast colonies were irradiated on beerwort agar, but that sodium chloride did not. Nadson (1925) postulated that x-radiation stimulated the rate of living of organisms. Stimulation of *S. ellipsoideus* by small doses of radiation is denied by Lacassagne and Holweck (1930). Old cells were more sensitive than young cells, and a change in temperature did not change sensitivity. Burger (1931) reports 100 per cent killing in ten minutes with 35 kv., 10 ma. at 3 cm. with radiation of about 0.35 Å. Lower voltages had no appreciable effect. The effects of x-radiation and ultra-violet radiation are compared by Nadson and Stern (1931), who found that the young cells are more sensitive: the vacuole contour changes first, then the metachromatin coagulates and the cell dies. Ultra-violet radiation caused more rapid death. A curious oligodynamic action was also described by these investigators.

Wyckoff and Luyet (1931) irradiated old cultures of a pure strain of *S. cerevisiæ* and found that the survival curves were of the type representing a multiple-hit-to-kill hypothesis. Many cells divided once, and in other cases separation failed and giant fusion cells were formed. Imshenetskir (1932) found 40 per cent of a 24-hour culture of *S. cerevisiæ* killed by 10 H.E.D. and that certain dyes gave a photodynamic sensitization to the roentgen rays. Holweck and Lacassagne (1930) summarized their findings on the yeast *S. ellipsoideus*.

Irradiation of yeast, after the beginning of fermentation, was found by Schneider (1925) to reduce the carbon dioxide production. Zeller (1926) stated that x-radiation produced a latent change in the cell substance, shown by increased sensitivity, but had no effect on the fermentation enzyme within the cell. An increase in the rate of carbon dioxide production was observed by Gronchi (1931) to be proportional to the intensity and was inversely proportional to the wave length. Each radiation was adjusted to 45 minutes with from 300 to 2,000 r and wave lengths of 0.55, 0.37, and 0.16 Å. Fardon and his co-workers (1936) stated that a substance liberated into the

[1] Through the kindness of Dr. G. Failla and a grant from the Atypical Growth Study Unit of Yale University it was possible to test the effects of radiation on yeast in the Biophysics Laboratory of Memorial Hospital, New York City. The hospital staff attended to the problems of radiation, which left the author free to measure the growth of the yeast. I am greatly indebted to Dr. Paul S. Henshaw for arranging the work in the laboratory so efficiently.

medium might account for the effect of the radiation.

Genetic variation producing new strains was believed by Nadson and Philippov (1928) to result from x-radiation of yeast.

Washed beer yeasts were irradiated by Wels and Osann (1925) and the growth of the populations was checked by 35, 38, 63, 77, and 88 per cent, respectively, after one, two, four, four, and eight hours of radiation (one hour equalled 12 H.E.D.). Neither the oxygen uptake nor the carbon dioxide production was affected, as measured by the Warburg technic. Large amounts of radiation are believed to produce an immediate death of the cell, while somewhat less radiation may cause a delayed death after one or more divisions of the cell (Lacassagne and Holweck, 1930; Lacassagne, 1930).

Fardon, Norris, and Ruddy (1936) found a variation in the effects of x-radiation and ultra-violet on the respiration of yeast. This was not due to the age of the yeast or the *p*H of the culture medium. They believe that the injured cells secrete a substance, or that the radiation activates a substance which stimulates the respiration of the remaining yeast.

The problems of radiation effects and the types of lesions have been summarized by Lacassagne (1934) and by Crowther (1938).

Consequently, the effect produced may appear differently, depending on how and when the growth of the yeast was measured and the next step in the analysis should be toward standardized procedures.

II

The rate of growth of a yeast population in an adequate and effectively constant environment is constant (Richards, 1928). When the population starts in a given amount of culture medium, the environment becomes progressively unfavorable and ultimately the growth is limited because of the exhaustion of food and the accumulation of injurious waste products. These changes have been measured for the pure strain of *Saccharomyces cerevisiæ* which Hansen obtained from a single-cell isolation (Richards, 1932, 1934).[2] While several criteria of growth are necessary to obtain a complete picture (Richards, 1933), one or more may be used in a given experiment, provided their limitations are kept in mind.

The most generally used criterion is the number of cells present in a given volume, often $^1/_{250}$ cu. mm., at a given time, obtained by averaging the counts of several samples made with an hemocytometer (16 small squares). The errors of the hemocytometer method for blood counting have been discussed by Berkson, Magath, and Hurn (1935). With care, the overall error may be reduced to about 4 per cent for yeast populations. Unless information is available showing the proportion of the cells of various sizes from recently formed buds to fully grown cells, the cell count does not give complete information as to the amount of yeast substance present. Other criteria have been used and the interrelations of some of these have been described (Richards, 1934) and a more complete analysis will be published later.

The optical density of a suspension of yeast cells may be readily measured by a photo-electric nephelometer (Richards and Jahn, 1933). When I is the amount of light transmitted to the photo-electric cell by the medium and I_t the amount transmitted by a population of cells in the medium at time t, then the optical density,

$$D = \log I_t - \log I = \log (I_t/I).$$

With the Richards and Jahn instrument, the number of micro-amperes generated by the light may be used as a direct measure of I. The nephelometric criterion is dependent on the number of cells present, the proportion of cells of each of the various sizes, and the condition of the cell protoplasm and wall. The values of D are a sort of inclusive measure of the yeast

[2] Used by Richards since 1928, and furnished to others. Some seven years after the isolation, a transfer sent to Dr. A. E. Navez duplicated the author's previous growth curves, which indicates the stability and reproducibility of the growth when the conditions are comparable.

growth, which is difficult to correlate directly with a single specific criterion such as cell number. The measurements are slightly more precise than counting, when the greater part of the population is within the light beam.

The instrument consists of a 100-watt projection bulb mounted in a lamp house to direct the light through a block onto a suitably screened photo-electric cell. The block is drilled at right-angles to the beam and so made that a test tube, containing a yeast culture, can be replaced in the instrument in the same position. Recent improvements of the original instrument are the addition of a ballast tube to lessen the fluctuations of the 110 v. lighting circuit, the use of a G.E. Blocking Layer type of photo-electric cell and a Weston No. 600 micro-ammeter with a mirror and a knife-edged pointer.

The yeasts are grown in Williams' medium, consisting of 20 gr. cane sugar, 3 gr. ammonium sulphate, 2 gr. potassium dihydrogen phosphate, 1.5 gr. asparagine, 0.25 gr. each of anhyd. calcium chloride and magnesium sulphate, and 1 liter of distilled water. Ten milliliters were placed in 2 × 15 cm. Pyrex test tubes and sterilized in an autoclave for 15 minutes at 12 pounds. This amount of heating does not affect the sugar, but repeated sterilization should be avoided. It is desirable to test the test tubes with culture medium and reject those which do not give the same reading on the photo-electric nephelometer. The maximum crop or yield, in 10 milliliters of medium, will depend somewhat on the chemicals used, hence it is advisable to start with sufficient stocks so that all the experiments of a given series will be made with the same chemicals. Merck's reagent grade chemicals were used in the experiments reported here except that the asparagine was Merck C.P. and the sugar was "Jack Frost." Any good table sugar may be used, although different brands of sugar will give some variation in the yields of yeast. The variations in growth, due to impurities present in the chemicals, are more or less well known. When it is necessary to change chemicals, a careful comparison should be made between the new and the old.

The yeast used should be a pure strain from a single-cell isolation, preferably of a well-known culture. The yeast used in these experiments is available as No. 4360 of the American Type Culture Collection. The stock strain may be kept on Difco malt extract agar or wort agar slants, by transferring about every four months. The transfers and inoculations should be made with the usual precautions used in bacteriology to avoid contamination. The yeast should be grown in a constant-temperature incubator at about 28° C. to avoid any special effects of higher temperatures (Richards, 1928).

The seed yeast used in an experiment should not be older than within the logarithmic phase of growth, in order to prevent the confusion of any lag period.

The growth then will continue for a period of time at a constant rate which is demonstrated by a straight line when the logarithm of the growth is plotted against time or when arithlog plotting paper is used. This period is called the logarithmic period and is readily duplicated and experiments made with yeast in this phase of growth are directly comparable. After the phase of constant rate of growth, the rate gradually decreases and an equilibrium number is attained by the population. A second smaller cycle of growth may follow the first. As the equilibrium is reached, the distribution of cell sizes changes from a preponderance of small cells to larger cells. In old populations the cells gradually change into resistant cells. These changes have been described for this strain of yeast (Richards, 1932). Old cells should not be used in experimental work because of the difficulty of determining their exact physiologic condition, and of duplicating the same population from experiment to experiment.[3]

[3] Precautions necessary for the use of yeast growth when testing the effects of various influences on it have been stated and discussed by Richards and Taylor (1932).

The number of cells can be counted with a hemocytometer without dilution. Care should be exercised to shake the tubes until the suspension is uniform and to place the sample in the counting chamber before settling takes place. The chief sources of error are: not taking representative samples and the difficulty of counting the cells when they are clumped together. Cells on the borderlines of the groups of 16 small squares, counted as a unit volume, are counted on the lower and right sides only, or else on the upper and left lines only. Practice will make possible consistent counts on the same population.

With the photo-electric nephelometer, some method of adjusting the light (rheostat or rotatable lamp house) is useful to make the reading without any culture tube assume arbitrarily chosen value. Otherwise, the readings of the population will have to be adjusted to a constant reference value. The tube must be inserted into the block in the same position, *e.g.*, with the Pyrex trademark toward the operator, or small imperfections in the glass will give variations in the readings. By shaking the tubes with a combined rotary and lateral movement, it is possible to obtain a uniform suspension without wetting the cotton plug. Should the x-radiation alter the optical density or kill the cells selectively with respect to size, this criterion alone will be inadequate to evaluate any effect observed.

III

Two wave lengths were available in these experiments. One set of experiments (Series 153) was made with 9,500, 19,000, 28,500, and 38,000 r at 70 kv., 30 ma., 95 *P. V.* with a 0.015 mm. celluloid filter over the cells. The distance from target to the culture was 18.6 cm. The other experiments were made at 200 kv., 30 ma., *P. V.* 169, with a 0.1 mm. copper and the celluloid filter, and the distance from the target to the cells was 33.6 cm. Both of these machines were standard equipment of the hospital.

During the radiation, the culture was poured into a container made by cementing celluloid to an embroidery frame. This permitted a thin layer and lessened the effects of secondary radiation. A similar, but slightly larger, container was inverted over the culture to avoid infection. Both were sterilized by scrubbing with alcohol before use, but making certain that none remained to affect the cells. A sterile, drawn-out, capillary pipette was used to transfer the culture back to the test tube. This method made it possible to wash the surface of the irradiation chamber with gentle pressure so that after some practice virtually all of the cells could be recovered. During the radiation, the cultures cooled, and to control this effect on growth the control cultures were treated in a similar manner and exposed to room temperature for the same length of time.

Some of the medium without cells was given 38,000 r and then inoculated with yeast to determine whether or not the radiation had any effect on the medium: no difference was found between the growth in the irradiated medium and the control culture.

Four series of tests were made with 200 kv. radiation with the following dosages: 200, 500, 1,000, 4,700*, 9,500*, 1,200, 14,220*, 19,000, and 38,000 r. (Those marked with an asterisk were duplicated, otherwise time permitted only one series at each of the amounts of radiation.) The results showed the irregularities expected with single tube experiments, but conditions beyond the writer's control prevented the originally planned repetition of the experiments.

Small amounts of radiation have relatively little effect on the growth of this yeast and the findings of Series 158 serve to illustrate the results of the experiments. The plots of the number of cells in $^1/_{250}$ cu. mm. (Fig. 1-*A*) show that the population decreased after the x-radiation and that the decrease was greatest for the greater irradiation, except that the early changes vary in time. The same effect was found for all dosages and for both wave lengths used. Later the size of the populations damaged by the x-radiation increases to

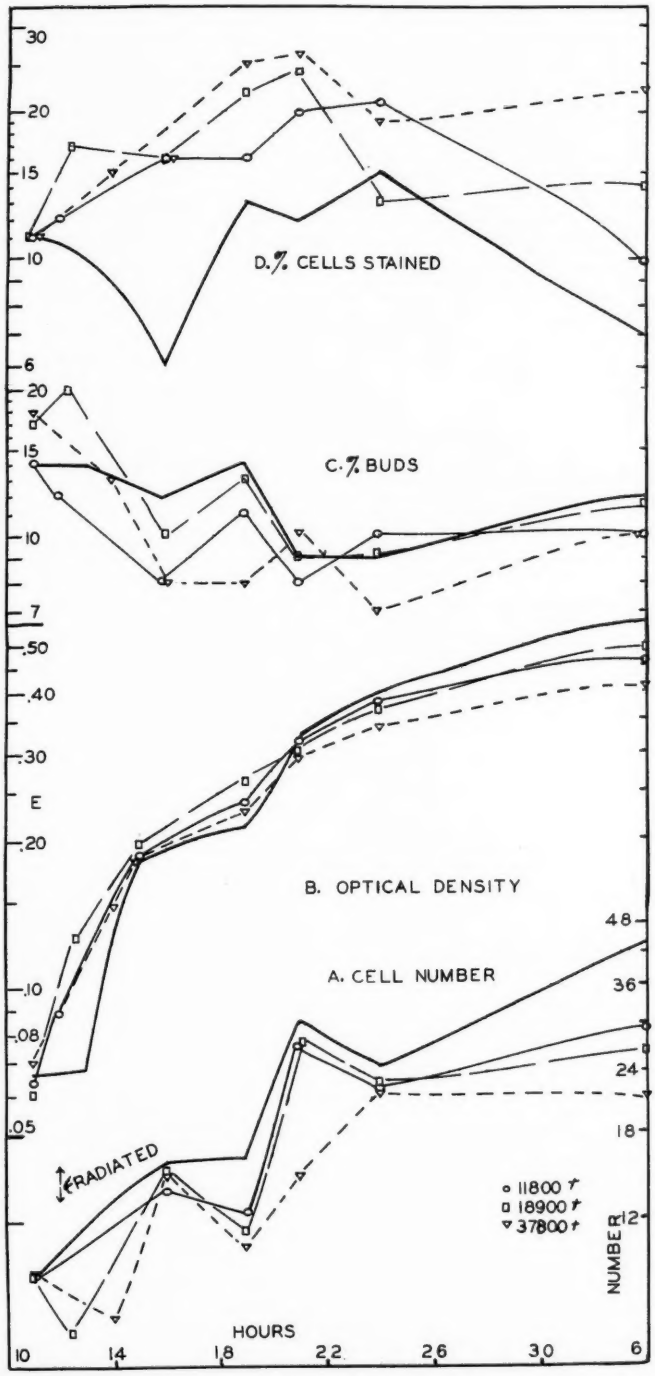

Fig. 1. *A*, Increase in number of yeast cells; *B*, Increase in optical density; *C*, Percentage of buds; *D*, Percentage of cells staining with methylene blue (*cf.* text). Smooth line is unirradiated control.

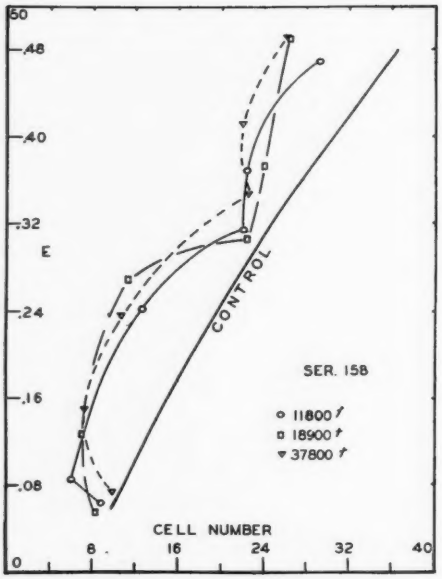

Fig. 2. The relation between number of yeast cells present per unit volume and the optical density of the population measured with the nephelometer.

nearly the same level of equilibrium as the controls at the end of the growth cycle. Two criteria of the effect of the radiation could well be the length of time following radiation until the relative rate of growth became the same as the control population, and the amount of reduction in the population size at a given time after the irradiation. With so few experiments, it is premature to state these values, but further experimentation should make possible the determination of the constants for different amounts of radiation.

The optical density, measured by the nephelometer (Fig. 1-*B*), shows that there was a greater density in the irradiated cultures for about nine hours following exposure and then the density became less than that of the controls. During the logarithmic period, the distribution of cells of different sizes present in the cultures is the same. Less cells are present in the irradiated cultures and, as will be shown later, less buds are present; therefore, the x-radiation must make the content of the cells more dense so that less light passes through them than through the control cultures. The populations receiving more than 15,000 r show an optical density less than that of the control populations.

The optical density and cell number are compared in Figure 2. The control culture shows a regular increase in the optical density corresponding to the increased number of cells in the population. The optical density of the irradiated cells is greater and reaches a maximum at about nine hours after exposure to the x-rays. The difference decreases, then increases, and at the end of the growth cycle becomes about the same as the controls for the same number of cells in the populations.

The percentage of buds is a measure of the birth rate and is plotted in Figure 1-*C*. The percentage of buds decreases markedly after irradiation and reaches about the same value as that of the controls by about twenty-five hours following irradiation. The effects showed considerable variation within and between the experiments, but in no case showed any stimulation of bud formation. The decrease in buds accounts for part of the lesser number of cells present in the populations after irradiation.

There is, unfortunately, no satisfactory easily performed test for dead cells. Culture of the individual cells is the only certain method of showing that they are or are not able to reproduce, although they may still live. Break-up of the cells apparently takes place shortly after death, and little evidence of them remains in the medium as the materials liberated are used in part by the remaining viable cells. Cells injured or moribund become deeply stained by methylene blue when a drop of a 0.5 per cent solution is added to four drops of the culture. The validity of the staining criterion is questioned,[4] but it remains a generally accepted means of evaluating the healthiness of the cells.

The percentage of stained cells is shown in Figure 1-*D*. More and more of the ir-

[4] A discussion and literature references to the staining of injured cells is given by Richards (1932). Dr. P. S. Henshaw's experiments, subsequent to the author's, indicate that methylene blue staining may not be as useful for the study of x-radiation injury.

radiated cells are stained for about nine hours following the exposure to x-rays, then the number decreases and ultimately approaches the level of the control populations at the end of the growth cycle. The changes in the protoplasm, which result in staining, are also probably responsible for the increased optical density. The minimum difference between the optical density of the controls and the irradiated cells (Fig. 2) occurs at the time of maximum staining.

IV

Neither the optical density (nephelometric) criterion of growth nor the increase in the numbers of cells present in a unit volume of culture medium alone is adequate to evaluate the effect of x-rays on yeast growth. The information of each assists in the interpretation of the observations. A complete study should include also the determination of the volume of cells present and the numbers of cells of different sizes.

The counts were made at intervals of about three hours after the exposure to the x-radiation until late evening, and then three times a day until the population equilibrium was reached following the second cycle of growth at about one hundred hours. The data given in Figures 1 and 2 were taken at three-hour intervals from carefully drawn, but not smoothed, plots of the observed growth. Much of the irregularity in the growth was due to the cooling of the cultures while they were out of the incubator during the withdrawal of the sample for the count.

If the injured cells divided once and then died, the curves showing growth on the arithlog plots would be moved over and then closely parallel that of the control populations. This could not have happened to any great percentage of the yeasts in these experiments. The staining criterion shows that a large proportion of the injured cells were buds. This double type of killing would account for the lack of systematic variation in the plots of Figure 1.

The effects with time on a growing population will be different from those on a population suspended in saline or other medium which will not support growth. Cells growing at a potentially unlimited constant rate will probably behave differently from old cells recovering from the adverse effects of an unfavorable environment. These factors must be considered and controlled in studies on survival.

The staining of the cells injured, and the lack of it by the normal cells, suggested that this, coupled with the reduction of the methylene blue to methylene white by the yeast populations, might be another measure of the effect of x-radiation on growing yeast cultures. A given amount of the dye was added to the irradiated and control cultures and the amount of reduction measured with the nephelometer at the end of 25 minutes. The following differences in the reduction of the dye were obtained with two series: 4,000 r, 19 units; 12,000 r, 22 units; 18,000 r, 18 units of optical density. Roentgen rays do affect methylene blue when the exposure is direct (Stenström and Lohmann, 1934; Stenström and Street, 1935).

V

To compare the rates of growth the relative rates (dy/ydt) were computed for the cultures at the same intervals of time[5] and comparisons made by subtracting the relative rate of each irradiated culture from that of the control at the same time interval. The differences are shown in Figure 3. Values to the left of the central zero line show increased relative growth of the irradiated culture and those to the right show retardation in the growth of the irradiated cultures in comparison with the relative rate of growth of the control populations. The smooth lines are the values for number of cells present and the dotted lines show the data from the nephelometric criterion. Much irregularity is present, as is to be expected from the small number of experiments permitted while covering this range of dosage in the available time. The

[5] The methods and calculations are described by Richards and Kavanagh (1937).

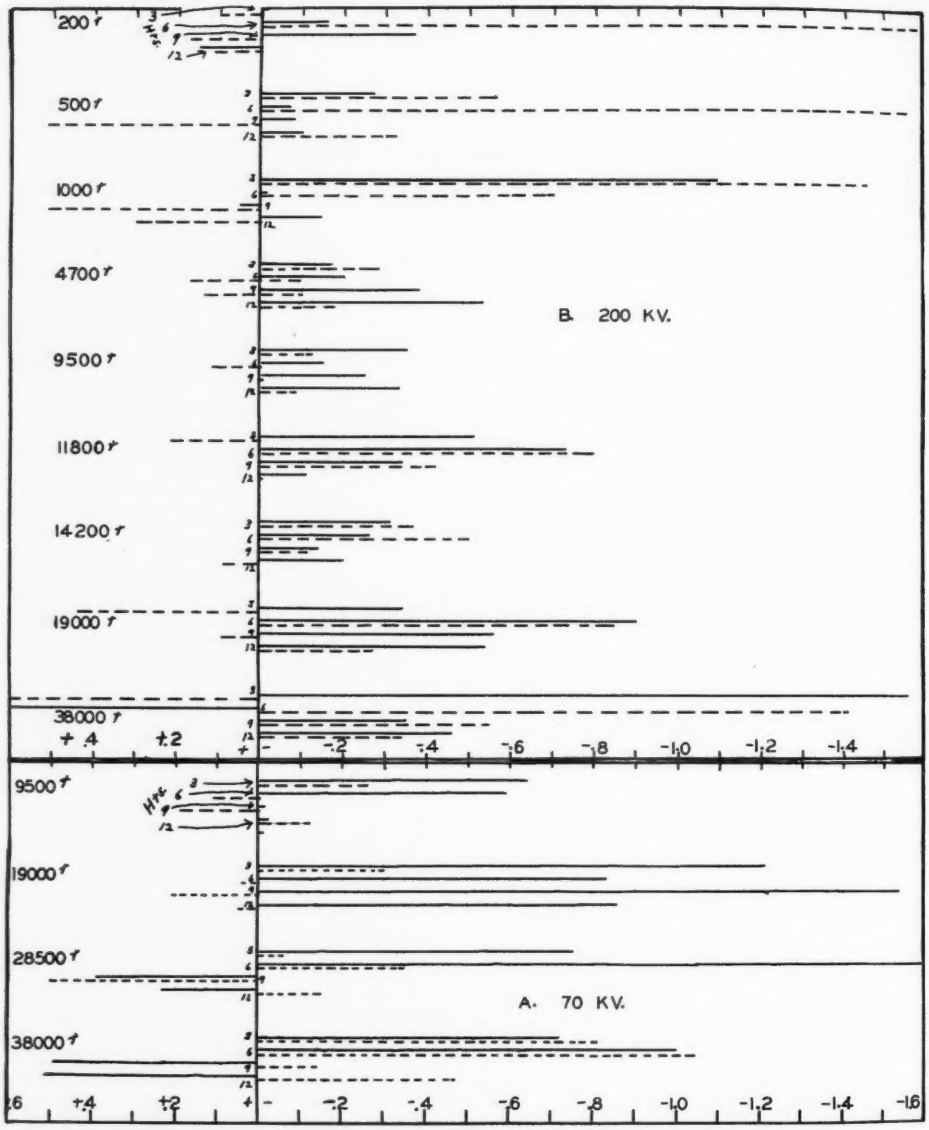

Fig. 3. The changes in relative growth rates following x-radiation. Solid lines, cell number; broken lines, optical density. The first two lines of each group show the difference between the relative growth rates of the irradiated and the control population at three hours after irradiation, the second at six hours after irradiation, etc.

200 kv. radiation gave little evidence of stimulation and there is very slightly more shown for the experiments with the 70 kv. radiation. Differences of less than 0.10 are probably not significant. Recovery from the effects of radiation occurs earlier with the two higher dosages of the 70 kv. radiation, which suggests that the cells are killed and the survivors less injured than appears from the 200 kv. irradiated populations. The lower dosages and the higher ones at 200 kv. are more effective in

retarding the growth rate of the yeast populations.

The survey experiments here reported show that several criteria of growth must be used simultaneously to analyze the effect of x-radiation on the growth of yeast. With properly replicated experiments, with a pure strain of yeast grown under appropriately controlled conditions, it is believed that yeast will be a useful test organism for the analysis of the effects of larger amounts of radiation and the clinical use of large amounts of radiation suggest that development of the methods outlined will be of value in experimental biology and medicine.[6]

SUMMARY

Populations of a pure strain of *S. cerevisiæ* were radiated with from 9,500 to 28,500 r at 70 kv., and with from 200 to 38,000 r at 200 kv. under carefully controlled, established conditions for the growth of yeast. The increase in number of cells per unit volume of culture is retarded by the x-rays. The growth measured with a nephelometer showed increased optical density for dosages up to 15,000 r, and decreased optical density for greater dosages. Recovery gradually takes place, and the irradiated cultures reach about the same equilibrium growth at the end of the growth cycles as do the controls. The percentage of buds and the percentage of cells stained with methylene blue are given. While a single criterion of growth may be useful, the analysis of the effect of x-radiation on yeast growth requires simultaneous information from several different methods for the measurement of yeast growth.

[6] The methods developed by Bliss (1935–1938) should assist in studies on the effect of radiation when sufficient data are available.

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THE INCIDENCE AND SIGNIFICANCE OF APICAL LESIONS IN PULMONARY TUBERCULOSIS: A PATHOLOGIC AND ROENTGENOLOGIC STUDY[1,2]

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and
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ALTHOUGH the various phases of pulmonary tuberculosis, including its pathologic and roentgenologic aspects, have for many years been favorite subjects of investigation, scarring at the apex of one or both lungs such as is so often present in lungs examined at necropsy, has received relatively little attention in the literature. That the lesion is tuberculous scarcely can be doubted, for Opie (1) observed evidence of tuberculosis in many cases, and Baldwin (2), Petroff (3), and Gardner (4) have stated that living bacilli of tuberculosis have been found in the lesion.

Examination for this lesion has been a routine procedure in the Department of Pathologic Anatomy of the Mayo Clinic for several years. The lesion is almost always at the extreme apex of one or both lungs (Fig. 1). It is seen as a whitish, opaque scar that stands out in contrast to the normal color of the apical visceral pleura surrounding the lesion. The portion of the apex covered by the scar varies considerably. It may be found, in minimal cases, as just a slight puckering and opacity or whitening of the visceral pleura. In extreme cases, the scarring may cover the entire apex, forming a cap. There are also many variations as to the shape it may take. It is interesting to note that it is never found where the rib has encroached on the lung. The thickness of the scar probably varies more than the surface extent. On sectioning the lesion, the thickness will vary from 1 mm. to 8 or 10 mm. (Fig. 2).

No evidence of a similar lesion of the parietal apical pleura adjoining this has been found except in cases in which adhesions joined the two layers of pleura at the point of scarring. Such adhesions were found in very few of the cases studied. On palpation of this area of the apex with the finger tips, the definite resistance of the scar compared to the surrounding normal apical pleura can at once be appreciated. In the less severely affected cases, the parenchyma of the lung directly beneath the scar is uninvolved; occasionally one will find an emphysematous cavity 2 or 3 mm. in diameter or multiple smaller ones.

On examining these apical scars with the aid of the microscope one sees a picture of complete fibrosis (Fig. 3). In many of the sections the connective tissue has become hyalinized. As a rule, there is no evidence of proliferation of blood vessels. In many of the sections in which there has been a general anthracosis of the lung, coal pigment will be found deposited in clumps between the connective tissue fibrils. Evidence that silicon might be interspersed with the coal dust is lacking when these areas are viewed through a polarizing microscope. Tubercle formation, giant and epitheloid cells are seldom seen.

The lesion is manifested roentgenographically as an opacity at the extreme apex of the lung (Fig. 4), its density varying considerably according to the extent of the scarring. It is seldom an obvious radiographic image, and to be sure that one is dealing with an apical scar the films should be stereoscopic and should be viewed in a stereoscopic viewbox. The lesion occurs almost always within the arc of the first rib and in the posterolateral quadrant

[1] Adapted from a thesis submitted by Dr. Addington to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Roentgenology.

[2] Accepted for publication in October, 1939.

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of the apical cupola (Figs. 5 and 6). The visceral margin is sharply defined and is usually slightly concave toward the lung-field. The density may be so slight that only the line of the visceral margin is seen to suggest its presence, and the average density is rather light. Occasionally evidence of calcium can be seen in the shadow. The opacity can never be seen to cross the first rib. Stereoscopically it appears to be just inside the first rib and is distinctly not a bony structure.

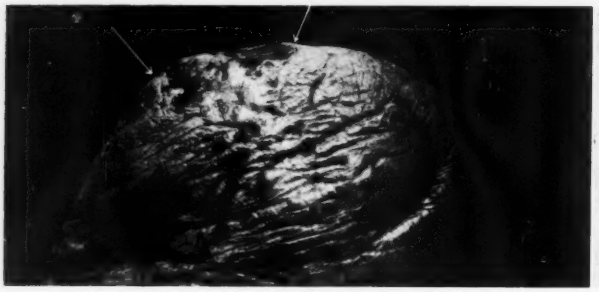

Fig. 1.

Fig. 2.

Fig. 1. Actual photograph of an excised lung with apical scarring.
Fig. 2. Thickness of apical scar as shown by actual photograph of excised lung. A section has been cut down through the middle of the scar.

Naegeli (5), in 1900, was the first to mention the existence of this type of tuberculous lesion. He made the statement that it could be found in practically 90 per cent of persons who had lived in cities on the continent of Europe, and who had died of causes other than tuberculosis. Opie (1) was the first investigator in this country to draw attention to apical scarring. He found it most often in patients in the later decades of life and believed it could be found in one out of every five or six adults dying from causes other than tuberculosis. He also found a great many of these lesions to be active, and at the same time, the primary complex to be calcified. Consequently, he believed this lesion to be a secondary type of infection derived from an exogenous source. During the World War he had the opportunity to perform necropsies on a number of British soldiers killed in action and he found evidence of healed tuberculosis of mesenteric nodes in many of these cases; he also found apical scarring with but a few having the calcified Ghon complex.

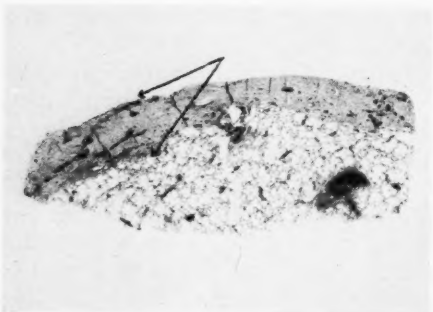

Fig. 3. Photomicrograph of a section through apical scar (× 8).

Van Zwaluwenburg and Grabfield (6), in 1921, investigated scarring at the apex from both the pathologic and the roentgenologic standpoints. They were quite well convinced that the lesion was closely associated with previous tuberculous infection of the tonsils or of lymph nodes in the cervical region. They believed that the tuberculosis bacilli gained access to the apical pleura directly by way of the lymphatic chain of the cervical region. They determined by roentgenogram that 93 per cent of the patients with tuberculosis of the tonsils had evidence of apical scarring and that 59 per cent of the patients with apical scarring had tuberculosis of the

cervical lymph nodes. In the large majority of patients on whom necropsy was performed they found evidence of adhesions between the visceral and parietal pleura.

On the other hand, Beitzke (7), in 1906, studying the routes by which the tuberculosis bacilli could enter the lung parenchyma, found no connection between the lymphatics of the neck and the cupola of the pleural cavity.

Grober (8), working along the same line of thought as Van Zwaluwenburg and Grabfield (6), injected the pharynx of dogs with India ink. The dogs were then killed (at intervals) and the lymphatics of the neck and apical cupola were dissected out to determine the dissemination of the ink. He found that it had been carried down the cervical lymphatics directly into the pleura of the apex. In some instances he found traces of the ink in the parenchyma of the lung beneath the apical pleura. From this study, he concurred with Van Zwaluwenburg and Grabfield that apical scarring was brought about in this manner and that this was possibly the route of infection in many cases of pulmonary tuberculosis. He postulated that the apical pleura offers a good deal of resistance to the bacilli and thus prevents, in the majority of cases, a parenchymal tuberculous infection. This, he thought, was the reason that apical scarring was such a benign lesion.

There is some evidence in the literature that the lesion may be the focus of an adult type of tuberculous infection. Fishberg, (9, 10), Allison and Medelman (11), and Pohle and his co-workers (12) have cited cases in which this has occurred. Allison and Medelman expressed the opinion that, in children, when the apical lesion is the focus, it causes a fulminating type of parenchymal tuberculosis.

The reported incidence of apical scarring in stereograms of the thorax varies a great deal. Pohle and his co-workers (12), of the University of Wisconsin, found evidence of scarring in 1.4 per cent of 2,072 students who had roentgenographic examinations of the thorax. Van Zwaluwenburg and Wickett (13) found that 10 per cent of patients registering at the University of Michigan Hospital had evidence of scarring at the apex. Andrus (14) found scarring in 27 per cent of a series of 1,085 stereoscopic films of normal adults.

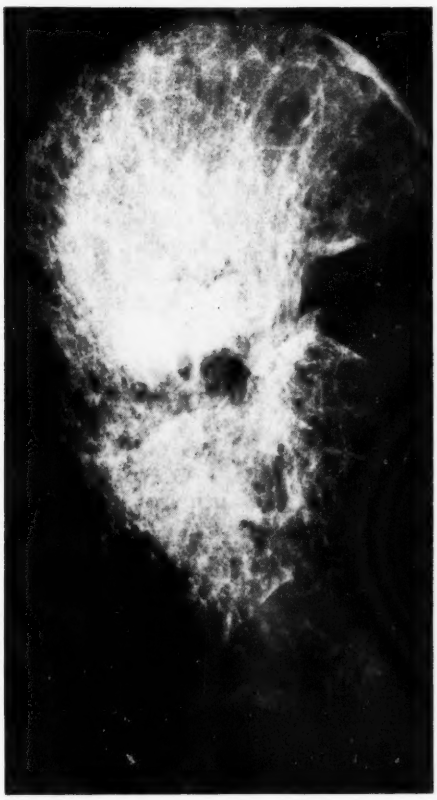

Fig. 4. Roentgenogram of an excised lung with apical scar. The scar is seen at the extreme apex on its medial margin.

Few who have studied this type of tuberculous lesion have ventured to explain the mechanism by which the scarring occurs. As one explanation, Opie and McPhedran (15) have expressed the opinion that this lesion is a secondary type of infection and from an exogenous source. In a study of scarring at the apex, Baldwin (2), Petroff (3), and Gardner (4), of the Trudeau Foundation, are of the opinion that the infection reaches the apex through the blood stream by way of the pulmonary

artery. They subscribe to the hypothesis that the hilus node, in the active stages of the primary infection, is unable to hold all the tuberculosis bacilli that lodge there and consequently that the bacilli are thrown off into the thoracic duct and thus into the pulmonary artery. They do not attempt to explain why the infection takes place only at the apex.

As this study progressed, it was seen that there was a definite correlation between the finding of calcification in the hilus nodes and apical scarring. Because of this correlation it was thought that, in conjunction with the study of apical scarring, a similar type of study of calcification of the primary infection in hilus nodes would be of value. Consequently both the excised lungs and the roentgenograms of the lungs taken prior to death were studied from the standpoint of the primary infection.

The incidence of primary infection has previously been studied by various investigators. However, the majority of these studies have been carried on among selected groups in various parts of the country. At the Mayo Clinic a fairly uniform cross-section of the rural and metropolitan population of the country is seen. Possibly a comparison of this study with a similar study made some years previously could be carried out to determine roughly the comparative incidence of primary infection.

The calcified, or caseous, hilus node is generally considered to be the most common evidence of primary tuberculosis. However, calcification of a primary focus must be distinguished from broncholiths, phleboliths, and calcific deposits in the bronchial, tracheal, or costal cartilages, or in old pyogenic inflammatory foci. Probably the most common opacity in the roentgenogram mistaken for calcification of the primary focus is that formed by the shadow of the cross-section of a blood vessel. Generally these are all readily distinguished from calcification of the primary focus.

Robertson (16), in a study of the incidence of tuberculosis in patients dying from causes other than tuberculosis, found evidence of it in 1,000 cases at necropsy, or 79.9 per cent. Opie and Andersen (17), in 1920, with the aid of roentgenologic examination, found in a large series of cases evidence of tuberculosis in practically 100 per cent of excised lungs examined in necropsy specimens more than 20 years of age.

Exact figures concerning the incidence of primary infection as found by roentgenograms of the chest are exceedingly hard to obtain. Farrell (18) found an incidence of 77 per cent in patients more than 14 years of age. Ickert (19), using a fluoroscope, found calcification of the primary lesion in 58 per cent of patients more than 14 years of age, and in 20 per cent of school children. Opie (20) has stated that approximately 20 per cent of normal adults will show calcification of the first lesion of tuberculosis in one set of anteroposterior stereoscopic roentgenograms.

Occasionally one will find an adult type of tuberculosis of the lungs with no evidence of a primary focus. It has been shown a number of times that the primary focus can heal without leaving any evidence of its having been there, or that the evidence may be so small as to escape observation.

From the clinical standpoint, probably the most important calcification in the thorax is in the child and the young adult. Robertson (21) has shown that tuberculous lesions in persons less than 30 years of age are found to be active three times as often as in persons more than 30 years of age. In the roentgenograms of 1,164 contact children, J. A. Meyers (22) was able to find calcification in 947. All of these children had been exposed to active tuberculosis. This is an extremely high percentage, especially for children, and shows the significance of calcification of the primary focus in children and young adults. From numerous studies of this sort it can be readily seen that calcification of the primary focus in young persons should be looked on with concern and an effort made to locate the source of the infection.

MATERIALS AND METHODS USED

The materials used in this study were taken from the Department of Pathologic Anatomy and the Department of Roentgenology of the Mayo Clinic. In order to obtain a large enough series of cases for this study the protocols of 350 necropsies performed in the last six months of 1936 and the first three months of 1937 were used, together with 330 additional necropsies personally observed by one of us (E. A. A.) during the period of the six months from April 1 to Sept. 30, 1937, inclusive.

At necropsy the excised lungs were first examined at the apexes for evidence of apical scarring. This could be determined by sight or by palpation with the tips of the fingers. The scar, if found, was then sectioned and the thickness of the lesion noted, and also the appearance of the parenchyma of the lung beneath. In the majority of cases a section was put in fixing solution to be stained with hematoxylin and eosin, and was later studied under the microscope. Next the hilar regions of both lungs in which no evidence of calcification in the nodes could be found were taken to the Section on Roentgenology and roentgenograms were made to determine if there was calcification that had been overlooked at the initial examination of the excised lung. In all cases, whether or not evidence of tuberculosis could be found in the hilus nodes, the spleen, liver, and mesenteric nodes were examined for healed tuberculosis.

Following necropsy the roentgenograms, if any had been made at the time of the patient's clinical examination, were reviewed for evidence of healed primary infection and of apical scarring. If there was no evidence at necropsy of healed primary infection or no evidence of calcification of the primary focus in roentgenograms of the chest, the plates of the pelvis or abdomen, if any had been taken, were reviewed to determine if there was calcification in the mesenteric nodes that had been overlooked at necropsy. All the

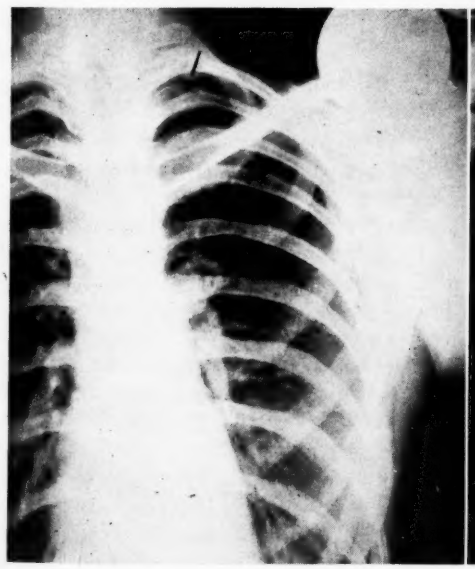

Fig. 5.

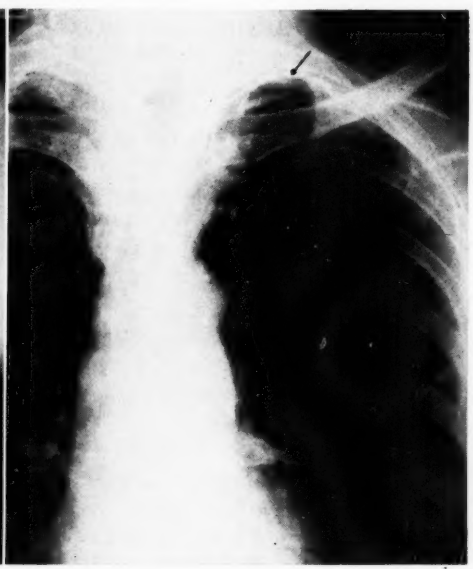

Fig. 6.

Fig. 5. Roentgenogram of chest showing irregular opacity at extreme apex which, at necropsy, proved to be an apical scar.

Fig. 6. Roentgenogram of chest showing calcification in an apical scarring which was proved at necropsy.

roentgenograms of patients whose necropsy records were obtained from the protocols were also reviewed to determine the presence or absence of apical scarring and healed primary tuberculosis of the lungs.

All the sections of apical scars taken at necropsy were examined microscopically to determine the activity of the lesion and the extent of the scarring. Many of the nodes in which tuberculosis could not be ruled out macroscopically were sectioned and examined microscopically.

RESULTS

The results of study of the excised lungs personally done coincide very closely with the statistical data obtained from the protocols; therefore, the statistical data in the tables and graph herewith include both studies.

Table I shows the number of necropsies in the various age groups and the percentage of cases of calcification of the hilus node in these groups. Out of this group, 582 roentgenograms of the chest were obtainable. In the 582 roentgenograms, calcification of the primary infection was found in 112, or 19.2 per cent. This includes either the hilus node or the Ghon lesion or both. In the 582, there were only 54, or 9.3 per cent, that had visible calcification of the hilus nodes in a single set of anteroposterior stereograms.

Table I also shows the incidence of apical scarring in the various age groups, the scarring being graded from 1 to 4. Grade 1 is minimal but shows definite scarring both macroscopically and microscopically, and Grade 4 is scarring which covers the entire cap of the apex and approaches 1 cm. in thickness. Among the 582 roentgenograms, there was definite scarring in 92, or 15.8 per cent.

Table II demonstrates the incidence of scarring when no calcification of the hilus node could be found. In 12 instances it was possible to make a roentgenogram of the region of the hilus, and in no instance was calcification of the hilus node found. In two instances calcification of the mesenteric nodes was found both in roentgenograms and at necropsy: in neither instance was calcification of the hilus node found. In only 62, or 9.1 per cent, of the 680 pairs of lungs excised was there no scarring when there was calcification of the hilus node.

In Figure 7 the percentages by age groups of calcification in the hilus node and of apical scarring are charted together to show how closely they follow each other.

There were 25 cases in which a calcified tubercle of both the spleen and the liver was found. In all except two of these cases there was apical scarring, and in both the latter there was calcified tubercule of the spleen alone. In all there were calcified nodes and in only one was there apical scarring. In three cases tuberculosis of the liver was found alone; in all three there were apical scarring and calcified hilus nodes.

In 12 cases there was an active adult type of pulmonary tuberculosis. In all except two there were scars of Grade 2 or greater, and in all except one there were calcified nodes. Of all the sections studied microscopically, only one showed evidence of activity in the apical scar (Fig. 6).

COMMENT

The inadequacy of the roentgenogram to portray the evidence of primary healed tuberculosis in the chest has been brought out in this study. It is far inferior to the skin test and, of course, to the examination of the excised lung at necropsy.

From Table I it is seen that the incidence of tuberculosis is lower in the younger than in the older age groups. This means either that a greater immunity to the tuberculosis bacillus is developing in the younger age groups, or that they are not coming into contact with tuberculosis bacilli as often. If the incidence of tuberculosis is compared with a similar study carried on in this department in 1923 and 1924, it is quite evident that there is a definite decrease. The two studies were carried out in practically the same manner. There is a decrease in incidence from 79.9 per cent to 64 per cent in this 13-year period. At the time of the study in 1923 and 1924 the

Ghon complex was the sole evidence of primary tuberculosis looked for and apical scarring was not considered.

The most frequent site of healed primary tuberculosis found at necropsy is commonly stated to be the calcified or calcareous hilus node. However, the healed lesion at the apex of the lung was the most common lesion found in this series of excised lungs. Among possible reasons for this contradiction is that the scarring at the apex is a lesion which can be seen and felt readily, but the calcified hilus node is often difficult to find. Calcification in the hilus node is frequently pin-head in size and could easily have been overlooked, even with the aid of a roentgenogram of the hilar region. It is probably a scientific impossibility to find all the evidence of healed primary tuberculosis in a lung. If it had been possible to make roentgenograms of each hilus region in the cases in which no calcification was found, the frequency of healed hilar tuberculosis would probably have approached that of apical scarring.

As has been pointed out by various investigators, the presence of a Ghon complex in the child and the young adult should be looked on with a certain amount of apprehension. This was brought out in two cases in this series in which two young persons who died of tuberculous meningitis had calcareous hilus nodes and Ghon tubercles, both noted by roentgenogram. The finding of calcification in the roentgenogram in each case of this type should be an added aid in the diagnosis. Many more of the calcifications in the hilus nodes could be seen on the roentgenogram if oblique views were also taken.

From Figure 7 it can be seen that calcification of the hilus node and apical scarring have very much the same type of curve. Apical scarring occurs five times more often with hilus node calcification than it occurs without it. From this it can be seen that there possibly might be a direct connection between these two manifestations of tuberculosis.

The scarring has no apparent direct connection with the Ghon tubercle, for the latter is in the middle or lower lobes in more than 50 per cent of the cases. In two cases found in this study the Ghon tubercle was 2 to 3 cm. from the apex, yet there was no evidence of apical scarring.

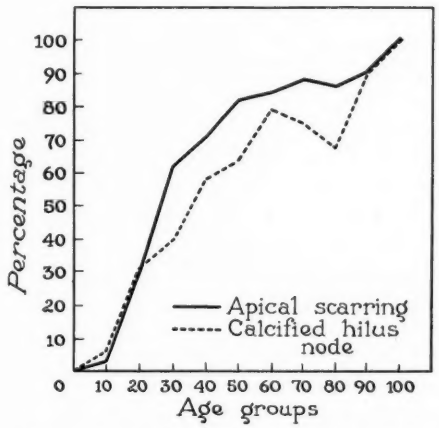

Fig. 7. Percentages by age groups of apical scarring and calcification of the hilus nodes. The same general curve is seen for both.

Opie and Andersen (17) expressed the opinion that apical scarring is a secondary exogenous infection, mainly because they found it active more often than the hilus node and also because it occurred later in life than the primary infection with its calcified hilus node. This study has brought out two counter-arguments to this conclusion, namely, the apical scarring has been found to be notably benign, and the apical scarring has been found just as often as calcification of hilus nodes in the earlier age groups, if not more often. The only explanation for these discordant findings is the fact that Opie and Andersen's (17) investigations were carried out 17 years ago and in a metropolitan area.

Apparently there is also a correlation of healed miliary tubercles of the spleen and liver with the calcified hilus node and apical scarring. In 25 cases in which healed miliary tubercles of the liver and spleen were found, only two did not have apical scarring, and only one did not have a calcified hilar node. In all seven cases in which tubercles of the spleen were found

alone, there were healed hilus nodes, and all except one had apical scarring. Apical scarring and calcification of the hilus node were found in all five cases in which healed tubercles were found in the liver and not in the spleen. It is interesting to note in this connection that the apical scarring in these cases was more extensive than that commonly found.

To prove scientifically the route of tuberculosis bacilli in gaining access to the apex would be a difficult task and is beyond the scope of this paper. However, a number of facts brought out in this study seem to imply that the infection is lymph-borne. Some investigators have expressed the opinion that the infection is brought about by retrograde lymph flow, due to obstruction of the lymph channels caused by the primary infection. No scientific demonstration of this type of infection has ever been made under the conditions of velocity and pressure that exist in the living body. To find foci of infection peripheral to the node is by no means evidence that the infection occurred by retrograde course. If this did take place, it would seem that it would have to do so by successive implantation of foci and thus, by continuity, run backward against the lymph flow. However, in this type of spread these foci are not found along the lymphatic channels, as Baldwin (2) has shown.

There is a possibility that apical scarring may occur from an exogenous source by an air-borne route, as Opie (1) has suggested. However, a number of points brought out in this study contradict this hypothesis. There is little doubt that apical scarring is a secondary infection and thus the tuberculosis bacillus is implanted in an allergic lung. The pathologic picture is one of a healed diffuse exudative process. It is not the well circumscribed lesion such as is seen in the healed primary parenchymal lesion of tuberculosis. It has been shown a number of times that it takes comparatively large amounts of tuberculosis bacilli to set up an infection in such a lung, and it does not seem possible that 76 per cent of the population would inhale enough bacilli to cause such an infection. The majority of air-borne infections in allergic lungs are first seen in the infraclavicular regions in the outer quadrant of the lung-field and not in the extreme apex.

The possibility that tuberculosis bacilli are brought to the apex by way of the blood stream should be considered. This would adequately explain many of the observations in this study as well as those of other investigators who have become interested in apical scarring. In the past little attention has been paid to the thoracic duct as a medium for the spread of infection. Washburn (23) has recently shown that spread of infection by this channel really does occur. It seems highly probable that a lymph node in the hilus of the lung during the active stage of the tuberculous infection could become so engorged with tuberculosis bacilli that it would be unable to hold them, and consequently some of them would be passed over into the thoracic duct. It has been shown that

TABLE I.—INCIDENCE OF CALCIFICATION IN HILUS NODE ON GHON TUBERCLE AND OF APICAL SCARRING BY AGE

Age Groups	Number of Necropsies	Percentage of Calcification	Instances of Special Scarring Grade				Total	Percentage
			1	2	3	4		
1– 9	33	6.0	1	0	0	0	1	3.0
10–19	26	30.7	7	1	0	0	8	30.8
20–29	50	40.0	25	5	1	0	31	62.0
30–39	67	58.2	33	10	5	0	48	71.6
40–49	120	62.5	63	32	2	2	99	82.5
50–59	147	79.5	67	50	6	1	124	84.4
60–69	160	75.0	65	65	10	1	141	88.1
70–79	66	79.6	28	22	7	0	57	86.4
80–89	10	90.0	3	3	2	1	9	90.0
90–99	1	100.0	0	0	1	0	1	100.0
Total	680	64.0	292	188	34	5	519	76.3

even in the calcified hilus node, active tuberculosis bacilli can be found in 20 per cent.

Sweany (24), in a study of tuberculous lymph nodes in all stages of tuberculosis, points out that it would be easy for the bacilli to get into the pulmonary circulation. Once the tuberculosis bacilli are in the thoracic duct they are carried directly into the pulmonary artery by way of the subclavian vein and throughout the entire lung-field.

Tuberculosis of the joints, kidneys, liver, and spleen is commonly thought to be brought about by bacilli being carried there in the blood stream, and it is probably no more illogical to postulate that the tubercle bacilli are carried to the apex in this manner. Why the bacilli do not set up miliary tuberculosis when the bacillemia occurs has never been explained. The selective localization of the tuberculous infection at the apex has long been a subject of scientific investigation. No one of the various investigations has established, to the satisfaction of all, the reason why tuberculosis selects the pulmonary apex.

TABLE II.—INCIDENCE OF APICAL SCARRING WITHOUT CALCIFICATION OF HILUS NODES

Grade	Number	Percentage of Instances of Apical Scarring of this Grade
1	87	29.8
2	30	16.0
3	4	11.8
4	0	0
Total	121	23.3

The possibility of poor lymphatic drainage at the apex has also to be considered in this connection. Miller (25), in a study of the lymphatics of the lung, has shown that the periphery of the lung parenchyma drains toward the pleura and not toward the hilus. In this study the apical scarring was never found on the visceral pleura where the first rib compressed the pleura and the immediate lung parenchyma. Also, it is known that tuberculosis may infect any part of the lung that has its lymphatics blocked by general silicosis.

The correlation of tuberculosis of the

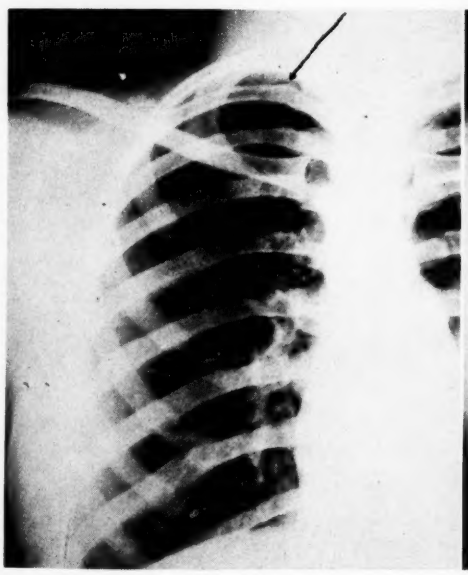

Fig. 8.

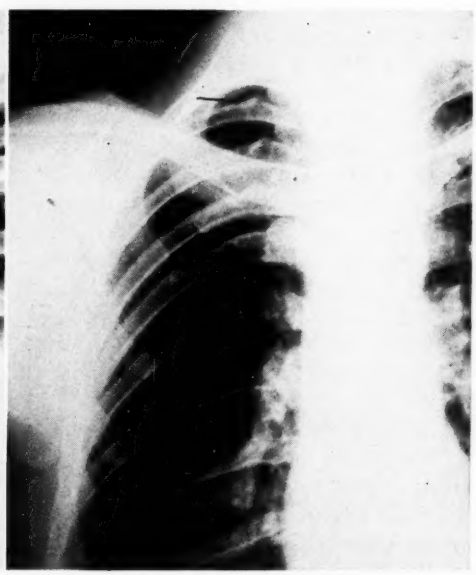

Fig. 9.

Fig. 8. Roentgenogram of chest showing the shadow of the subclavian artery.
Fig. 9. Roentgenogram of the chest showing the shadow of Sibson's fascia.

tonsils and cervical nodes with apical scarring is probably better explained by the infection following the lymphatic channels that drain into the right lymphatic duct and thoracic duct than by the manner in which Van Zwaluwenburg and Grabfield (6) and Grober (8) believed it reached the apex. It is not probable that two layers of adjoining pleura could be infected and still so few cases occur with adhesions between the two surfaces.

If the explanation of apical scarring as a result of infection through the blood stream is accepted, then apical scarring could be brought about by almost any focus of tuberculosis in the body. There were 121 cases in which it was not possible to find calcification in the hilus node in conjunction with the apical scar. Possibly the source of the apical lesion in some cases was in the tonsils, the cervical nodes, or the mesenteric nodes.

It has been shown by experimental study in animals that tuberculosis bacilli are carried into lymph channels and the vascular system by macrophages. It is then possible for tuberculosis bacilli to gain access to the arterial circulation and thus set up minute infections in the liver and spleen. Why the bacilli localize in the spleen and liver in the majority of cases can be explained only on the basis of selective localization.

From the roentgenologic standpoint, the apical lesion is overlooked in the majority of cases. The portrayal of apical scarring in the roentgenogram is definitely a different shadow than that of an old healed fibrotic parenchymal lesion and should not be confounded with such an opacity. Seldom is calcification seen in an apical scar.

However, there are two structures at the apex that might be confounded with apical scarring. The first is the shadow of the subclavian artery (Fig. 8). This shadow is a homogeneous opacity with a sharply defined lower border, concave downward. It is seen beneath the third rib posteriorly on the left side; however, it may also be seen on the right side. If the roentgenogram is made with the tube centered over the mid-chest, the shadow of the artery may be seen closer to the second rib posteriorly. A vertical continuation passing to the aortic arch medially is often seen.

The other confusing structure is Sibson's fascia (Fig. 9). This fascia extends from the transverse process of the seventh cervical vertebra on the same side to the inner margin of the first rib. It is seen only within the arc of the first rib and in the posterolateral quadrant of the apical cupola. The direction is forward and outward, and rather more anteroposterior than lateral. The visceral margin is sharply defined and is usually slightly concave toward the lung-field. The density may be so light as to be hardly visible. The shadow can never be seen to cross the first rib, and on stereoscopic examination it is distinctly not a bony structure.

SUMMARY

An infrequently studied tuberculous lesion of the pulmonary apexes has been described. Its possible connection with other healed tuberculosis in the body is also considered. Apical scarring, as reviewed in the roentgenogram, must be distinguished from normal apical structures. There appears to be a general decline in the incidence of primary tuberculous infection in the chest.

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OSTEOPETROSIS: A CASE REPORT[1]

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OSTEOPETROSIS (syn. marble bones, *Marmorknochenkrankheit*, osteosclerosis fragilis generalisata, Albers-Schönberg disease) is a disease primarily characterized by increased density and thickness of the cortical and spongy portions of the bones with encroachment on the medullary cavity. It involves the entire skeleton. Roentgenologically it is distinguished by increased opacity of the bones which appear heavy and lacking in structural detail. The posterior clinoids are usually thickened and clubbed, the skull bones show increased density, and there are frequently peculiar alterations in the contours of the long bones. There is often a concomitant anemia of the myelopthisic type with enlargement and myeloid changes of the spleen, liver, and lymph nodes.

Multiple fractures are frequently found; occasionally osteomyelitis, optic atrophy, hydrocephalus, and subarachnoid hemorrhage are other more or less frequent manifestations of the disease.

The condition was first described by Henck in 1879, and first demonstrated roentgenologically by Albers-Schönberg in 1904. In 1934, McCune and Bradley (5) presented a review of the literature up to 1933 and reported a case. In their review they cited 68 cases, including their own case and two reported after their paper was accepted for publication.

Since 1933 we have been able to find reports of seven other cases (2, 3, 6, 7, 8, 9, 10).

McCune and Bradley stated that in eight cases there were complete, and in four, incomplete, autopsies. In their case rather comprehensive clinical studies were possible but autopsy was denied.

The following case is presented to add another to those recorded, and to present the autopsy report. Unfortunately the postmortem examination was necessarily incomplete in regard to the osseous system.

The male child, J. P. H., was brought to the Wisconsin General Hospital in a moribund condition. The case history was summarized by Dr. K. B. McDonough, of the Department of Pediatrics, and the pathologic findings follow.

The patient, one year of age, was admitted to the pediatric service of the Wisconsin General Hospital on April 18, 1936. The history, obtained from the mother, stated that she and the child's father were 40 and 39 years of age, respectively, and in good health. There were four siblings, in age 15 to three years, all in good health. There was no history of syphilis, tuberculosis, or blood disease. The infant was born at full term; delivery was spontaneous. The child was very blue at birth and held its head in a "funny" position. He cried with short staccato cries, which did not sound normal, whenever anyone tried to straighten up his head, which was held well back. The infant became jaundiced shortly after birth. This jaundice was present off and on throughout the first year. The infant weighed seven and one-quarter pounds at birth. He had always been under the doctor's care, and seemed to have fever and chills at various times for no apparent reason. He had had convulsions at intervals and these had increased in frequency and severity during the past two months. He was breast-fed for three months and vomited a great deal but the vomiting was not projectile in type. He received a simple milk mixture after the age of three months and was started fairly early on orange juice and cod liver oil. He had also received some vegetable soup and oat meal gruel. These were started late in the first year because the

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infant was unable to eat well. He was unable to sit up and had difficulty in holding his head up. He did not grow as the other children had during the first year of life. The infant had always been constipated and appeared to be unusually irritable. He had a tendency to hold his arms at a peculiar angle behind his head. The mother thought that the baby experienced some pain when his arms were extended or an attempt was made to put him in a sitting position. It was thought that the infant had grown paler during the past two or three months.

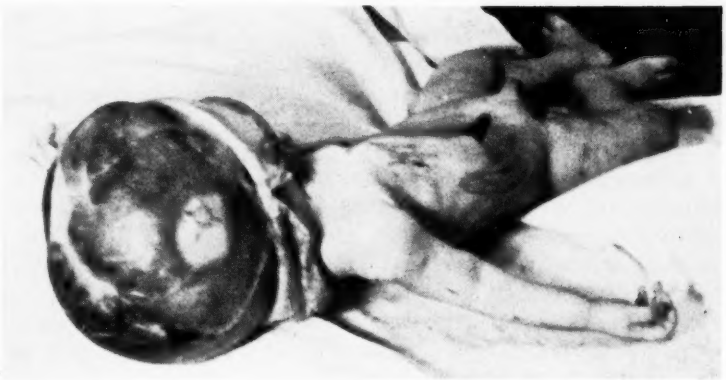

Fig. 1-*A*.

Physical examination showed a very pale, markedly undernourished infant who appeared small for his age. His head appeared large in proportion to the rest of his body. He had a definite Mongoloid facies. The eyes were widely spaced and there was a slight exophthalmos. The facies was not that of a hydrocephalic infant. There was a yellowish pallor of the skin. His length was 25 inches. The head was rather large, measuring 47 cm. The anterior fontanelle was open and measured 4 × 5 cm.: the remainder of the fontanelles were closed, as were also the suture lines. The skull felt thick to percussion and a flat note was elicited throughout. The left occipito-parietal region was prominent. Examination of the eyes showed the extra-ocular movements to be normal. Vision was apparently normal. The fundi could not be seen. There were no teeth, although the upper gums were swollen. Excessive lymphoid tissue was present in the pharynx. The infant breathed through his mouth. The ears were normal. The neck was held rather rigidly and when the infant was raised to a sitting position he held his head erect and cried loudly. The

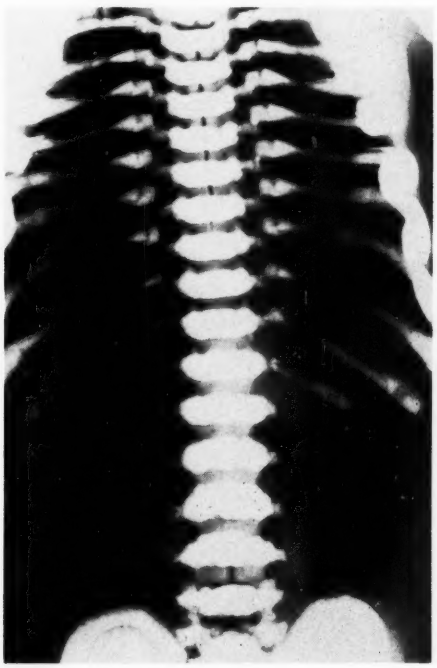

Fig. 1-*B*.

anterior and posterior cervical lymph nodes were enlarged. The thyroid was not palpable. The chest was symmetrical but expansion seemed to be limited. The costal margins were flaring. The heart and lungs were normal to physical examination. The abdomen was prominent. The spleen was firm and smooth, and palpable to the crest of the ilium. The liver edge was palpable 5 cm. below the costal margin. There was a generalized adenopathy. Examination of the extremities showed no limitation of movement and the infant was able to kick and grasp objects without difficulty. The wrists and ankles were not enlarged. Neurologic examination showed all the reflexes to be hyperactive. During the examination the infant had a convulsion, lasting about one minute, which was characterized by opisthotonos and tetanic spasm of all the extremities. Before any laboratory studies or x-rays could be obtained, the infant experienced a very severe convulsion. He became very cyanotic and before measures could be instituted to stimulate respirations, the infant expired.

AUTOPSY

The body was that of an emaciated male infant 64 cm. in length. Enlargement of the cervical, axillary, and inguinal lymph nodes was noted, and these nodes were soft. The abdomen was distended. The spleen was considerably enlarged and weighed 210 gms. The cut surface was dark red and firm. The pulp was apparently increased in amount, and the malpighian corpuscles were not visible. The liver was somewhat enlarged, weighing 730 gms. The cut surface was pale with a slight yellow tint. The mesenteric lymph nodes were enlarged and soft.

The bone of the skull was 8 mm. thick, dark red and mottled in appearance. There was organizing hemorrhage between the skull and the dura, and these had to be

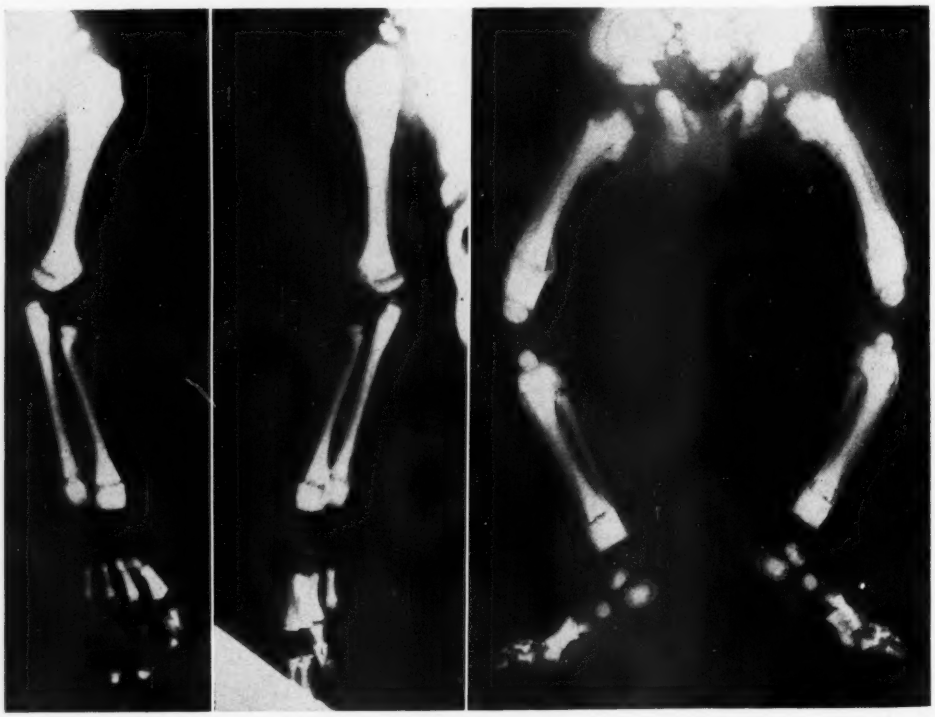

Fig. 2-*A*.

Fig. 2-*B*.

separated by blunt dissection before the calvarium could be removed. Except for a well marked edema of the leptomeninges over the frontal and parietal lobes, the brain showed no pathologic change.

The bones of the whole body were increased in density. The cortex was thickened and the marrow cavities were almost completely filled by a network of heavy bony trabeculæ.

Essential Microscopic Findings.—The lymph nodes, spleen, and liver were the sites of extra-medullar blood formation, clusters of primitive cells being found in all these organs. Eosinophilic myelocytes were especially prominent.

The femur could be sectioned only after long decalcification. The cortex was thick and the medullary cavity was almost completely filled by heavy, bony trabeculæ. In some fields there were irregular areas of newly formed bone, staining blue with hematoxylin and eosin. The bone marrow was scanty, and in some places was replaced by fibrous tissue. Cellular detail was not well preserved on account of the long decalcification necessary, but here and there one could recognize an osteoclast. Groups of osteoblasts were also present.

Anatomical Diagnosis.—Idiopathic osteosclerosis (Albers-Schönberg's disease), with compensatory myeloid change in the lymph nodes, spleen, and liver.

COMMENT

Several roentgenograms were obtained before and after the postmortem examination (Figs. 1–3). The roentgenograms exhibit findings similar to those of the case of McCune and Bradley (5). These authors should be consulted for a complete discussion of the findings. There is in this case the additional roentgenographic finding of markedly increased thickness of the right parietal region with localized tumefaction (Fig. 3-*B*), general increase in the thickness of the skull, and increased density and lamellation of the periosteal or pericortical new bone.

The lack of similarity of the roentgenographic picture in the infant and in the older child and adult is probably associated with alterations in the activity of bone formation incident to growth. It is evident in this case, also, that the changes began *in utero*, and that at or about the time of birth some alteration in the pathologic process occurred. The presence of scurvy need not be hypothecated, and rickets is unlikely. A parallel striation of the metaphyseal portions of the long bones is very distinct. Not stressed previously are the perpendicular striations of the "rims" of the ilia and the texture of the skull. Clubbing of the clinoids is particularly evident in the anterior processes. On the original films of the skull a thin line of periosteal

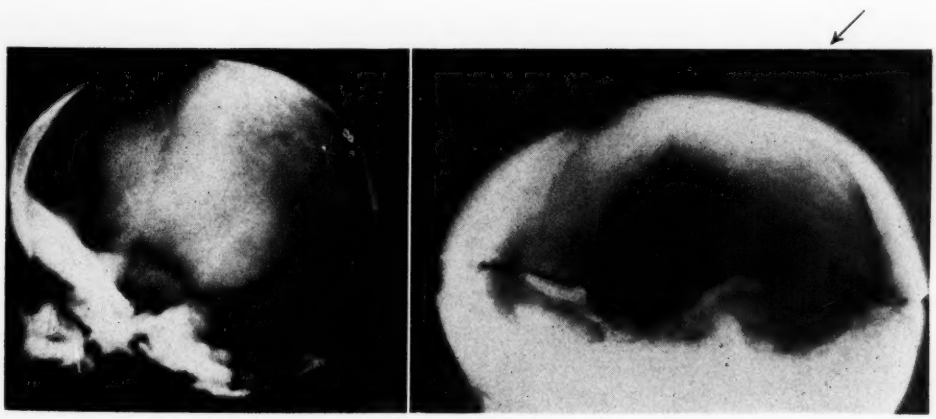

Fig. 3-*A*. Fig. 3-*B*.

new bone formation similar to that about the shafts of the long bones is evident.

The disposition of the density in the vertebral column is interesting.

The recently published reports (1–10) on the association of fluorine intoxication and osteopetrosis in the adult suggest roentgenologic investigation of infants and children in regions where fluorine ingestion is known to be considerable. The data in this case are insufficient to determine the possibility of fluorine as an etiologic factor.

The possibility that cases such as the one presented and of infants with similar findings represent an entirely different disease of distinct pathogenesis from the adult types must not be disregarded.

SUMMARY

1. A previously unreported case of osteopetrosis in an infant is presented, with the pathologic findings and a series of illustrative roentgenograms.

2. There is some question as to whether all cases reported as osteopetrosis fit into a common clinico-pathologic syndrome.

3. Investigation of infants and children in regions where some degree of fluorine ingestion is known to occur is suggested as one means of determining the etiology of this condition.

4. Periosteal involvement is, contrary to statements in the literature, present in this case.

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BENIGN DUODENO-COLIC FISTULA

WITH REPORT OF TWO CASES[1]

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DUODENO-COLIC fistula is a rare finding and of the few cases reported in the literature only two have been described as being due to benign lesions; it is an abstract of these two cases which will be given in this paper. The other cases were all due to a carcinoma of the transverse colon perforating into the duodenum. Other cases may have been reported in connection with other lesions of the gastro-intestinal tract, but I have been able to find only two cases reported under the heading of "duodeno-colic fistula" from 1885 up to the present time.

The etiology of benign duodeno-colic fistula is usually a perforation of a duodenal ulcer into the transverse colon with a resulting fistula between the two. Other benign lesions may cause a fistula between the duodenum and colon, but none could be found reported in the literature. The absence of a typical history of duodenal ulcer does not exclude this as the cause, for we are all familiar with cases of duodenal ulcer in which the only sign or symptom of the ulcer may be a sudden hemorrhage, with subsequent roentgenography demonstrating the presence of an ulcer though the patient still presents no real symptom of the ulcer except for the hemorrhage.

The fistula may involve any part of the duodenum because of the close relationship between the duodenum and the transverse colon.

Ulcers of the second and third parts of the duodenum are probably more common than is generally realized. Hauser (1), using the combined statistics of five authors on the location of *perforated* duodenal ulcers, lists 274 as being located in the first part, 12 in the second part, and five in the third part. This indicates that almost 6 per cent of perforated duodenal ulcers are located in the second or third part of the duodenum. These figures are probably high for a general average, as there may be a greater tendency for ulcers of the second and third parts of the duodenum to perforate than for ulcers of the first part. These figures, however, do indicate that ulcers of the second and third parts of the duodenum are more common than we realize. Accurate statistics on the frequency of ulcers beyond the first part of the duodenum are not available, because ulcers here are more difficult to detect roentgenologically than in the first part and they are usually not operated upon unless they perforate.

The patient with a duodeno-colic fistula may or may not give a history of a sudden abdominal pain. A persistent diarrhea with rapid loss of weight, in spite of a voracious appetite, is quite typical of a duodeno-colic fistula. This history is common for any fistula between the colon and the upper gastro-intestinal tract and is not specific for a duodeno-colic fistula.

Blondeau and his co-workers (2) reported a case of a 55-year-old man who came to them for an incorrigible diarrhea, the yellowish liquid containing undigested alimentary débris. His symptoms were not very pronounced, there being merely a feeling of some epigastric heaviness after meals. He had sometimes, but not always, colicky pains but without much suffering, and without the insistence of his family would not have been roentgenographed. On examination there was noted a pronounced emaciation but with no evidence of an intra-abdominal tumor. The liver was hard and slightly enlarged. A barium meal showed rapid emptying of the stomach. The first few mouthfuls of the meal

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entered the duodenum rapidly and cascaded into the transverse colon. About 90 per cent of the meal passed into the transverse colon, with the remainder passing through the duodenum into the jejunum. In one hour the stomach was empty. There was definite tenderness to palpation at the sub-hepatic angle. Operation was advised but was refused by the patient. During the following two months the diarrhea became less severe and the patient improved generally. The following month he presented signs of pyloric obstruction, confirmed by roentgenoscopy. He continued to refuse operation and died one week after the last examination.

This case, although it was not proved by operation, is included as it had been reported as a benign fistula. The history of the patient during the period of his observation and with the occurrence of pyloric obstruction are much against a benign fistula, and I believe this case was probably due to a cancer of the colon perforating into the duodenum.

Rees (3) reported a case of a woman 62 years of age, whose past history was negative except for typhoid fever 28 years previously. She complained of indigestion and a sense of weakness and soreness in the pit of the stomach, which had been present for eight or nine months. About two hours after meals she became distressed and complained of gas and occasional vomiting. Laxatives gave her temporary relief. She had lost 15 pounds in weight. A Graham-Cole test revealed no filling of the gall bladder. Roentgen examination with a barium meal revealed no evidence of pathology of the esophagus, stomach, or duodenum. The sphincter of Oddi was incompetent and permitted the barium to pass into the hepatic ducts. The colon was not examined with a barium enema. Exploratory celiotomy revealed slight thickening of the gall bladder but without

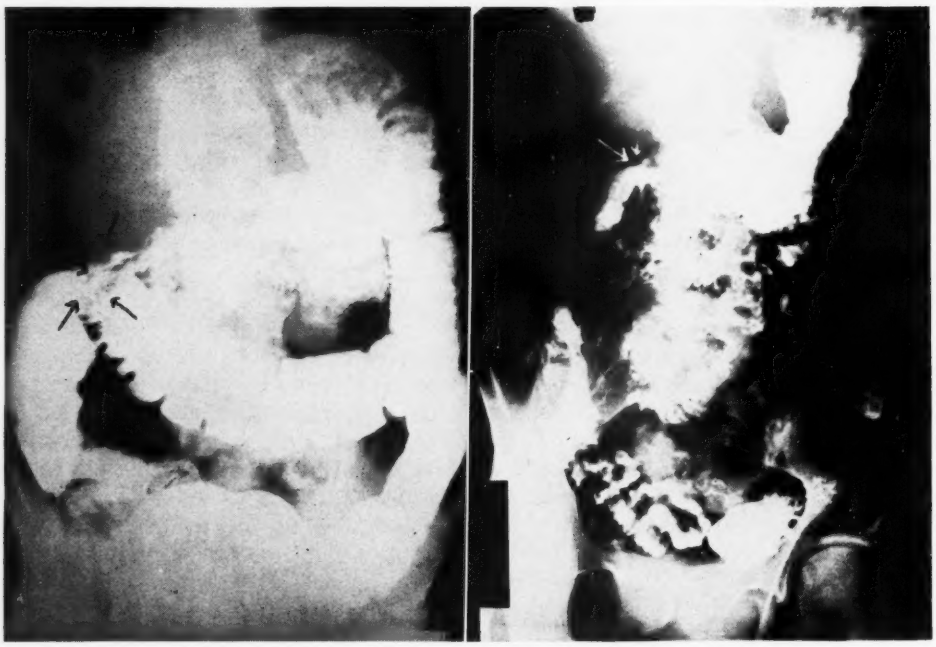

Fig. 1. Fig. 2.

Fig. 1. Case 1. A barium enema showing filling of colon, duodenum, stomach, and jejunum. Arrows indicate filling defect in the colon at the site of the fistula.

Fig. 2. Case 1. Roentgenogram made after evacuation of the barium enema. Note barium remaining in the stomach, duodenum, and jejunum. Arrows point to deformity of first part of duodenum by active ulcers.

gallstones. The common duct was dilated to about twice the normal size. A dense band of tissue was found extending anteriorly from the middle of the lateral aspect of the descending duodenum and the proximal portion of the horizontal duodenum to the upper border of the transverse colon. Further dissection revealed a fistulous tract, 5–6 cm. in length, extending from the transverse colon to the duodenum just distal to the ampulla of Vater. Microscopic examination of the excised fistulous tract showed the upper half of the tract to be lined with epithelium similar to that in the duodenum, while the lower half of the tract was lined with epithelium similar to that in the colon. Rees assumed that the fistula must have resulted from a perforation of an ulcer in the colon during the attack of what was thought to have been typhoid fever 28 years previously.

This case was not diagnosed by roentgen examination of the stomach and duodenum. If a barium enema had been given, it is thought that there would have been no difficulty in demonstrating the fistulous tract. This point, which has been mentioned previously in the literature on many occasions, should again be emphasized. Any fistulous tract involving the colon can be most accurately and easily detected if a barium enema is given. If the examination is limited to the barium meal, the fistulous tract may not be demonstrated. Although many fistulæ between the colon and the stomach or small intestine have been demonstrated with a barium meal, a failure to demonstrate the fistula with the barium meal does not exclude the possibility of its being present.

Of the above two cases abstracted from the literature, one was diagnosed on roentgen examination but was not confirmed by operation or postmortem examination, and the other one was not diagnosed on roentgen examination but was found at operation. The following two case reports are, as far as I have been able to find, the only two such cases which have been diagnosed by roentgenography and confirmed by operation. In the second case the roentgenologic and surgical diagnoses were confirmed by postmortem examination.

The two cases reported in the literature and also my two cases come within the "carcinoma age," and the probability of cancer must be differentiated from a benign lesion. The roentgen examination can strongly suggest the benign nature of the lesion, but a cancer cannot be definitely excluded except by operation. The accurate differentiation between a malignant and a benign fistula by roentgen examination is not essential, because surgery is the only method of treatment in either case and is necessary to establish the correct diagnosis.

After operative resection of the fistulous tract, the diarrhea disappears, the patient gains weight rapidly, and soon returns to normal health. The cure of these patients by surgery is quite dramatic.

REPORT OF CASES

Case 1. F. H., a 58-year-old Catholic priest, was referred to the Leonard Morse Hospital, Natick, Mass., on Nov. 2, 1931, for roentgen examination of the gastrointestinal tract. His chief complaints were loose, watery bowel movements and loss of weight.

When about twenty years of age the patient had a bilateral excision of the glands in his neck. The past history is otherwise unimportant.

Three years before entry (that is, in 1928), he began to have loose, watery bowel movements, usually occurring twice a day, with short intermissions up to the present time. There is no history of blood in the stools. Seven months before examination he began to lose weight and there was an onset of vomiting, usually waking him up in the night and occurring several times during the week. These attacks followed the eating of greasy or fried foods or on a day when he had had no bowel movement. The vomitus consisted chiefly of watery material but occasionally there were particles of food eaten at breakfast time, perhaps sixteen hours previously.

No blood was seen in the vomitus. He had lost about twenty-five pounds in weight during the seven months before his entry into the hospital.

Physical examination showed an extremely emaciated elderly man with a slightly injected pharynx, normal heart, lungs, and abdomen. The blood pressure was 85/50; the white blood count 5,300 per c.c.; the red blood count 2,500,000 per c.c., and the urine negative but with a renal function of 40 per cent.

Fig. 3. Case 2. A barium enema showing filling defect in the colon at the site of the fistula to which the arrows point. (*C*) colon; (*D*) duodenal cap.

Roentgen examination with a barium enema showed no evidence of pathology in the descending colon. In the transverse colon, just distal to the hepatic flexure, there was a filling defect and at this point the barium was seen to enter the duodenum at the juncture of the first and second parts and thence into the stomach with only a small amount of the barium passing into the colon proximal to this point (Fig. 1). The filling defect in the colon was at the point of the fistulous opening and it did not have the characteristic ragged outline usually seen in a carcinoma of this type. The patient was then allowed to expel the enema, after which, examination revealed a large amount of barium remaining in the stomach and duodenum (Fig. 2). Some of the barium had passed from the duodenum into the jejunum. A barium meal was then given but I could not see the barium pass from the duodenum into the colon through the fistula. The first part of the duodenum was deformed by an ulcer. The fistulous tract entered the duodenum just distal to the deformity caused by the ulcer. A diagnosis of a duodenal ulcer and a fistula between the duodenum and colon was made. The cause of the fistula was thought to have been a perforation of a duodenal ulcer into the colon or a perforation of a carcinoma of the colon into the duodenum.

The patient was referred to the Peter Bent Brigham Hospital, in Boston, for operation. A barium enema at that hospital confirmed my findings. The patient was operated upon by Dr. David Cheever and I am indebted to him for his permission to use his operative and follow-up notes, as follows: "A right paramedian incision was made. The liver appeared normal. The gall bladder was buried in adhesions. A hasty examination of the stomach and coils of intestine generally revealed nothing abnormal. Just distal to the pylorus there was marked deformity, with induration of the first part of the duodenum, and subjacent to this could be felt a definite small mass, deeply seated behind the colon. In order adequately to unravel and identify this it was necessary, first, to dissect the gall bladder free from adhesions by sharp dissection, mobilizing the second part of the duodenum from the posterior parietes and mobilizing the hepatic flexure of the colon, and to free the ascending colon from its connections. After this it could be demonstrated that the hepatic flexure of the colon was firmly attached to the first part of the duodenum by a tube-like structure about the size and thickness of a small pencil and about one centimeter

in length. After complete dissection it was possible to pass the finger completely around the fistulous tract. The adjacent colon felt normal. The first part of the duodenum, proximal to the fistula, was deformed and there were apparent traces of new ulcerations just distal to the pylorus, as well as the one which presumably caused the fistula by perforation, which was more on the inferior aspect of the first portion. The fistulous tract was ligated and divided with the cautery. A posterior gastro-jejunostomy was done in the usual manner."

The patient made an uneventful recovery. At the time of the operation he weighed 100 pounds. He gained nine pounds in weight while he was in the hospital and three weeks after his discharge from the hospital he had gained a total of 16 pounds. By the end of the first year after the operation he had gained over thirty pounds. At the last report, six years after the operation, he was in good health, and examination at that time revealed nothing abnormal. He had lost some weight during the last year but this I believed to be the usual loss which occurs with advancing years.

No microscopic examination was made as no tissue was removed at the operation. The six years of normal health following the operation I think definitely eliminate cancer as the cause of the fistula and the finding of acute ulcerations in the first part of the duodenum, at the operation, indicates also that the fistula must have been due to a perforation of a previous ulcer of the duodenum.

Case 2. R. H., the patient, a 46-year-old male machinist, was referred to my office on June 17, 1937, for roentgen examination of the gastro-intestinal tract by Dr. Thomas R. Donovan. His chief complaints were a severe diarrhea and a marked loss of weight.

The family and past histories were essentially negative.

For the past 15 years he has suffered from a persistent "indigestion," with irregular periods of freedom from symptoms. He has had pain in the epigastrium most of this time, which came on about one to one and one-half hours after meals and was relieved by eating food or by taking baking soda. He has not been under any regular medical treatment during this time. His greatest weight during this period had been 138 pounds. About one year previous to his visit to me he had developed a sudden, acute, agonizing pain in the epigastrium just at the completion of a 150-mile automobile trip. Upon reaching his destination he immediately went to bed, where he was attended by a physician who administered opiates to relieve the pain. Within a few hours the pain was relieved and by the end of the week the man felt much better and his previous digestive symptoms had disappeared. A diarrhea, between six and nine movements a day, began at that time, and he developed a voracious appetite. He ate large quantities of any food that was available, but, in spite of this, he experienced a rapid loss of weight and strength. For the six months previous to the present examination he had been under medical treatment for the persistent diarrhea, but examinations of his stools were always negative. The diarrhea has been so severe as to occasion pain and soreness in the rectum. He states that he has been unable to work for the past three years because of his illness. He has lost 46 pounds in weight.

Physical examination showed a man of middle age, emaciated to a marked degree. His weight was 94 pounds. His heart and lungs were negative. His abdomen was flat and not tender to palpation and there were no palpable masses. There was excoriation about the rectum, with marked painful spasm of the sphincter which prevented a satisfactory rectal examination. The remainder of the physical examination was negative.

The laboratory examinations revealed a normal urine; 6,600 white blood corpuscles per c.c.; 3,600,000 red blood corpuscles per c.c., and the hemoglobin to be 70 per cent (Tallquist).

Roentgen examination of the colon with

a barium enema (Fig. 3) revealed a smooth filling defect in the transverse colon distal to the hepatic flexure. At this point the barium column passed through a fistulous opening into the duodenum at the juncture of the second and third parts. The barium passed up the duodenum and filled the first part and some of it passed through the pylorus into the stomach. Some of the barium also passed through the third part of the duodenum and downward into the jejunum. Some of the barium passed by the fistulous opening and filled the hepatic flexure, ascending colon, and cecum. The colon distal to the fistulous opening was quite smooth in outline and lacked the usual haustral markings, but there was no evidence of an ulcerative colitis. After the patient was allowed to expel the enema, examination revealed a large amount of the barium to have remained in the stomach and jejunum. A barium meal was then given (Fig. 4), but I could not definitely visualize any of the meal as passing through the fistula from the duodenum into the colon. At this time there was excellent visualization of the colon at the site of the fistula (Fig. 5), yet there was no evidence of a ragged outline to the filling defect such as would usually be seen in a case of cancer. The filling defect was quite smooth in outline, was not palpable, and had the appearance of a benign lesion. A diagnosis of a duodeno-colic fistula was made and its benign nature was suggested to the patient's physician.

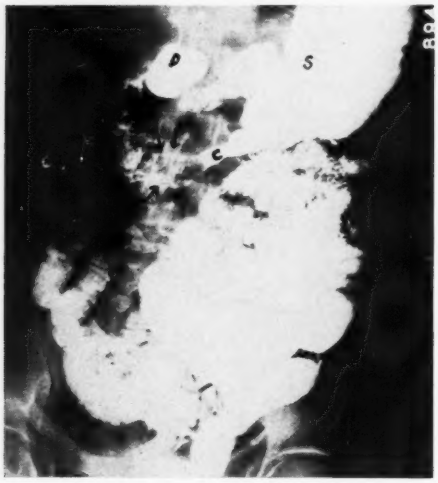

Fig. 4. Case 2. Roentgenogram made after evacuation of the enema which was immediately followed by the barium meal. The arrows indicate the site of the fistula. (*C*) colon; (*S*) stomach, and (*D*) duodenal cap.

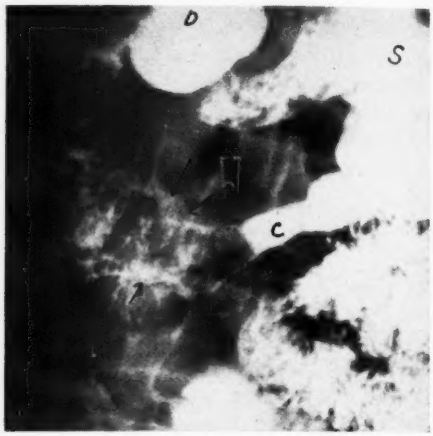

Fig. 5. Same as Figure 4 but showing localized area of fistula. Note the benign appearance of the colon at the site of the fistula.

He was operated upon five days after the roentgen examination. Under avertin-ether anesthesia, a high right rectus incision was made. The hepatic flexure of the colon was found to be embedded in a dense mass of adhesions, extending posteriorly and involving the third part of the duodenum and also the distal portion of the second part of the duodenum. The duodenum was quite long and mobile except at the juncture of the second and third portions, where a fistulous tract was found to extend from this part of the duodenum to the transverse colon near the hepatic flexure. The peritoneum was incised along the lateral aspect for a distance of about five centimeters, up to the area of the fistulous tract. After sharp dissection the fistulous tract was seen to be very short and the colon was found to be adherent at its posterior aspect to the upper aspect

of the duodenum. The fistulous tract was divided and the openings into the duodenum and colon were closed. The gall bladder was normal and was filled with easily expressed bile. There were no adhesions about it and, due to the marked emaciation of the patient, the cystic and common ducts were easily identified. The stomach was negative. There was no evidence of an ulcer or other pathology of the duodenum, except for the fistula. The patient had a satisfactory post-operative course for five days and the bowel movements had returned to normal. At this time he complained of pain in the lower abdomen and there was some elevation of his temperature. Rectal examination revealed marked tenderness anterior to the rectum. There was a moderate amount of bulging of the abdominal wall in the right lower quadrant. An incision was made in this area and a large abscess cavity was entered, filled with pus mixed with a brownish foul-smelling fluid. The abscess cavity was in contact with the cecum and extended upward along the ascending colon for a distance of about five centimeters. This cavity extended downward into the pelvis. The cavity was emptied by suction and drains were inserted. The patient did not respond satisfactorily and died twelve days after the second operation. A postmortem examination was performed. The duodenum and colon in the area of the fistula were removed and sent to a pathologist for examination, which revealed several small polyps in the colon near the site of the fistulous opening. No evidence of cancer could be found in the duodenum or colon.

This case gave a typical history of a duodenal ulcer for the past 15 years, with a sudden attack of pain which probably represented the perforation of the ulcer into the colon, as the diarrhea immediately followed this attack. There can be no question but that the fistula was caused by a perforation of a duodenal ulcer, and that the ulcer from which the patient apparently suffered for 15 years was located at the juncture of the second and third parts of the duodenum. The roentgen examination, the operation, and the postmortem examination all failed to demonstrate an ulcer in any other part of the duodenum or the stomach.

SUMMARY

Benign duodeno-colic fistula is a rare finding and only two cases could be found in the literature. One of these cases was not confirmed and, from its history, it was probably not a benign fistula.

The benign fistula is usually due to a perforation of a duodenal ulcer into the transverse colon and it may involve any part of the duodenum.

The diagnosis is not difficult if the colon is examined with a barium enema, but the fistula may not be demonstrated if the examination is limited to a barium meal.

The benign origin of the fistula may be suspected from its appearance on roentgen examination, but operation is necessary to exclude definitely the presence of a cancer.

Two cases are reported here which have been proved by operation and also, in one instance, by postmortem examination, to be due to a perforation of a duodenal ulcer into the transverse colon.

18 Hartwell St.

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DISCUSSION

JOHN D. CAMP, M.D. (Rochester, Minn.): There is very little I can add to this subject because I have never seen such a case and the records at our institution fail to disclose any such lesion on the basis of a perforated duodenal ulcer.

Dr. McPeak has emphasized the fact that it is impossible to determine the benign nature of this fistula prior to surgery and, of course, he also mentioned

that malignant disease is the most common cause of this condition.

Another not common but not rare cause of a fistula involving the colon is the presence of gall-bladder disease and pericholecystitis with the formation of a fistula between the gall bladder and colon. The duodenum is frequently involved in the inflammatory mass and, in the presence of such a condition, a fistula between the duodenum and colon—and possibly gall bladder as well—may occur.

If the roentgenologist cannot make the diagnosis of a benign fistula prior to surgery, it seems to me that the two cases which Dr. McPeak has mentioned have some very definite clinical evidence which may allow this distinction to be made. In the first place, both patients had a story which was quite typical of a duodenal ulcer, complicated by an acute attack of pain. Such a story, of course, is not common in the presence of malignant disease, and I think this is important in trying to establish the diagnosis, because the surgical treatment of this condition is necessarily a radical procedure, and if we can have some reassurance of its benign nature before operation, radical surgical procedures to effect a cure can be justified.

THE SIGNIFICANCE OF THE ROENTGEN VISIBILITY OF THE HORIZONTAL FISSURE[1]

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THE appearance in the roentgenogram of the chest of linear shadows corresponding to the interlobar fissures of the lung is not unusual, and by comparison of such shadows with anatomic specimens a better understanding of the anatomy of the lungs has been attained (10, 5, 24). This has permitted the more accurate localization of pathologic processes seen in the chest roentgenogram in terms of the lobes and fissures which may be involved. Particularly important has been the identification of certain previously puzzling shadows sometimes included among the "unresolved pneumonias," and which have, in some instances, been shown to be due to effusions limited to the pulmonary fissures. The unusual and, at times, bizarre outlines of these shadows are thus easily understood.

By means of its normal position in the horizontal plane, the fissure between the right upper and middle lobes has attracted primary attention in this extension of x-ray critique. Thus, it is obvious that the plane of a fissure which becomes partially radiopaque would more easily be demonstrable when its greatest diameter lay in the axis of the roentgen ray, whereas, if the ray should penetrate it perpendicularly, the result might be only a faint haziness in the area of its projection, difficult of evaluation, if even detectable. In the customary postero-anterior chest roentgenogram, the horizontal fissure is, therefore, in a position, despite its slight superior convexity, to cast its densest shadow, whereas the long or oblique fissures in front of the lower lobes, being intercepted perpendicularly by the x-ray in the greater part of their extent, are not usually noticed on the film unless they contain a considerable amount of fluid, or their walls are grossly thickened by pathologic induration. Such pathology might give rise to the unusual shadows referred to previously, correctly identified through an adequate understanding of pulmonary lobar anatomy, and by the study of the interlobar spaces, in the case in question, by unusual or special technic. At times the lateral extremity of the oblique fissure attains a plane passing anterolaterally from the hilus which permits it to be demonstrated in the usual chest radiogram as an almost vertical line or one passing slightly laterally and cephalad from the diaphragm, approximately one-fourth the distance from the lateral costal margin to the mid-line (Fig. 1). This shadow may be either unilateral or bilateral, and visualization is made possible by the occasional concurrence of the plane of the fissure and the more divergent rays from an x-ray target comparatively close to the film. A lateral projection, however, permits better demonstration of the oblique fissure of the hemithorax nearest the film, and, on the right, its relationship with the horizontal fissure (11). These demonstrations have been presented by several authors (2, 4, 10).

The accumulation of fluid in limited interlobar spaces has been described frequently (1, 6, 9, 13, 17, 18, 20, 21, 22, 23, 25), the usual rotund shadow requiring differentiation from abscess or primary or secondary cancer of the lung. Such accumulations have been accounted for on a hydrostatic basis in cardiac decompensation as a localized form of right pleural effusion, the remaining pleural space having been obliterated by adhesive pleuritis. They have also been considered, at times, to be of inflammatory origin complicating tuberculosis, pneumonia, or rheumatic fever. Practically all such accumulations reported are too well marked to be questionably pathologic, and their problem has been one of differential diagnosis among

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pathologic entities rather than distinction from normalcy.

Although, therefore, it has been recognized that gross shadows of particular location and conformation may represent pathology related to the pleural fissures and the fissural pleuræ, the significance of a much greater number of fine-to-coarse linear shadows in the areas of the fissures has remained in doubt. Particular debate has centered on the pathologic significance of such linear projections of the right horizontal fissure of the lung, which, due to its position, is particularly suited to demonstration without special technic. Some authors (2, 3, 4) have considered these lines to vary in significance only quantitatively from the grosser infiltrations or effusions in the fissures, and to have similar origin, hydrostatic, exudative, or proliferative, as the case might be. Others have considered at least the finer projections to represent the normal pleuræ, which they have thought capable of casting a roentgen shadow when viewed tangentially. Crecelius has been able to show such linear shadows of normal fissural pleuræ in roentgenograms of lungs removed from the chest through careful adjustment of the tangency of the central roentgen ray to the pleural surface (4). Inouye (8), on the other hand, considered the normal pleura incapable of casting a shadow despite tangency of the ray. Double lines occasionally are seen (Fig. 2), but have been considered to have a significance no different from single ones (2), the fissural pleura merely being tangent in two places to the plane of the roentgen rays.

Anatomico-pathologic correlations have, at times, shown pleural induration apparently to be responsible for the antemortem demonstration of such linear shadows, but in numerous instances no such correlation has been present, the pleura appearing quite normal at autopsy (4). In such instances, the linear roentgen images were assumed to be due to normal pleuræ, a view not taking into account a second possible explanation of apparent

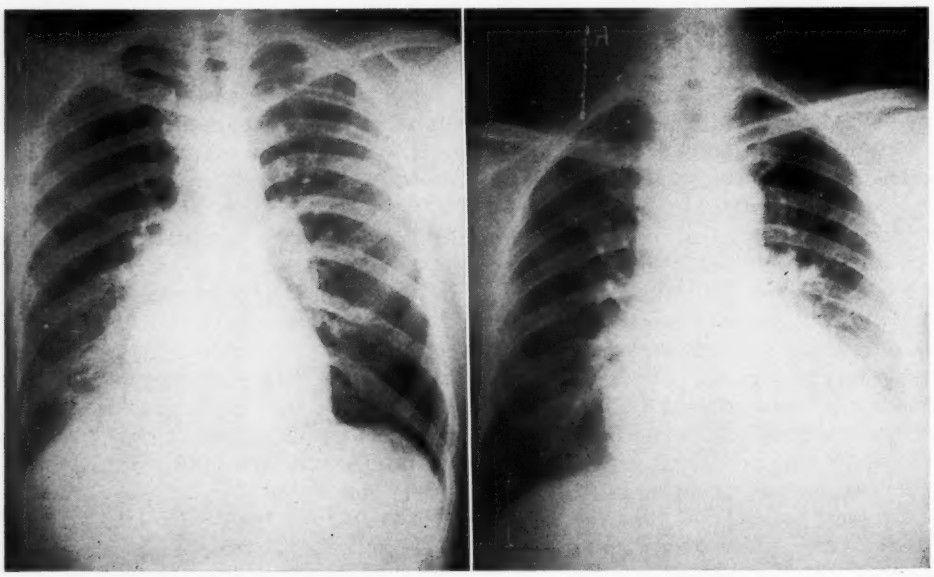

Fig. 1. Fig. 2.

Fig. 1. Roentgenogram showing Grade I visibility of right horizontal fissure, and enlargement of cardiac shadow

Fig. 2. Roentgenogram showing Grade I visibility of right horizontal fissure. Two parallel lines are noted, indicating tangency of roentgen rays to fissure along two planes.

normalcy, namely, an increase in the intrafissural film of pleural fluid responsible for an x-ray shadow *in vivo*, but insignificant, neither cardiac nor pulmonary pathology, and the incidence of linear shadows corresponding to the right pleural fissures

TABLE I

Fissural Lines	Normal Series 501 X-rays	Tuberculosis Series 162 X-rays	Cardiac Series 283 X-rays
Absent	80%	59%	48%
Present	20%	41%	52%
Grade I	20%	30%	45%
Grade II	0.2%	7%	6%
Grade III	0%	4%	0.8%

This table shows the absence or presence and grade of lines corresponding to right superior fissure, in roentgenograms of the chest of normal control series, of tuberculosis series—including cases with bilateral or right unilateral infiltration—and of cardiac series of chest roentgenograms showing enlarged hearts.

TABLE II

Right Superior Fissural Lines	Normalcy	Effusion	Congestion
Absent—137 X-rays	86%	6%	8%
Grade I—130 X-rays	73%	14%	13%
Grade II—14 X-rays	14%	60%	26%
Grade III—2 X-rays	0%	100%	0%

This table shows the occurrence, in chest roentgenograms with enlargement of cardiac shadow, of signs of passive congestion, of pleural effusion, and of normalcy, excepting the presence of fissural shadows.

or absorbed at autopsy. The scarcity of satisfactory autopsy material has limited the solution of the problem in this direction (4).

Although occurrence of such linear shadows has been noted by Crecelius (4) in "almost 50 per cent of cases," their preponderance in x-rays demonstrating tuberculosis, or cardiac enlargement, appeared impressive to the author, and an analysis of this occurrence was undertaken in an effort to determine in a manner not yet employed in this problem the significance of the shadow under discussion. The presence of fissural shadows had been noted previously in heart disease (7, 13, 17) and especially in chronic passive pulmonary congestion, but its incidence in a normal control series had not been determined. Lines of exudative, or of proliferative origin, had also been reported relating to tuberculosis (12), to rheumatic fever (19), and to other types of inflammatory infiltration (14), but again without normal controls.

Accordingly, to determine the normal incidence of such linear projections and the effects upon their occurrence of inflammatory and hydrostatic factors—which presumably were the chief modifying influences—three groups of x-rays were selected and studied as follows: 501 chest roentgenograms were selected, showing

was determined. One hundred sixty-two roentgenograms showing pulmonary tuberculosis involving the right lung, either alone or as a part of bilateral disease, were also examined for the incidence of these pleural lines. A third group of 382 roentgenograms in which the heart was definitely enlarged was reviewed, in a similar manner, the common denominator of cardiac enlargement being selected as the most dependable roentgenographic feature of cardiac disease and failure. Inspection of the hospital charts available in 211 of these cases demonstrated the dependability of this criterion. In all three series it was considered advisable to sub-group the linear shadows according to their fineness or coarseness, as suggested by Busi (2), to determine, if possible, any difference in significance of shadows of fine, medium, and coarse caliber. These calibers have been termed, respectively, Groups I, II, and III, and are illustrated by Figures 1, 3, and 4. Data relating to the incidence and caliber of the linear projections of the horizontal pulmonary fissure in these three series of x-rays are shown in Table I.

Examination of these data renders the pathologic significance of linear shadows of the right horizontal pleural fissure unquestionable, as well as the greater significance of the medium and coarse shadows over the finer projections. Thus, almost exactly one-fifth of otherwise normal chest roentgenograms showed linear shadows which in but one instance of 501 cases were of medium caliber, all the remaining pro-

jections being of the fine type and none of the coarse. Among the tuberculosis series, the incidence of lines was 100 per cent greater than normal, being found in 41 per cent of all roentgenograms, and with a definite shift toward the medium and coarse types of projection, which occurred in 7 per cent and 4 per cent of roentgenograms, respectively. Among the cardiac cases, the incidence of pleural lines was even higher, being 150 per cent greater than in the normal control series. Thus, 52 per cent of the roentgenograms of chests with cardiac enlargement showed the linear shadows, of which, however—as might have been expected—lower percentages were of the medium and coarse types of lines than among the tuberculosis cases. These occurred in 6 per cent and 0.8 per cent of x-rays, respectively. Acknowledging the occurrence of linear pleural shadows in 20 per cent of the normal series, their significance in favor of pathology is thus unquestionable, with a notably greater incidence of lines in association with an enlarged heart than even with tuberculosis of the right lung.

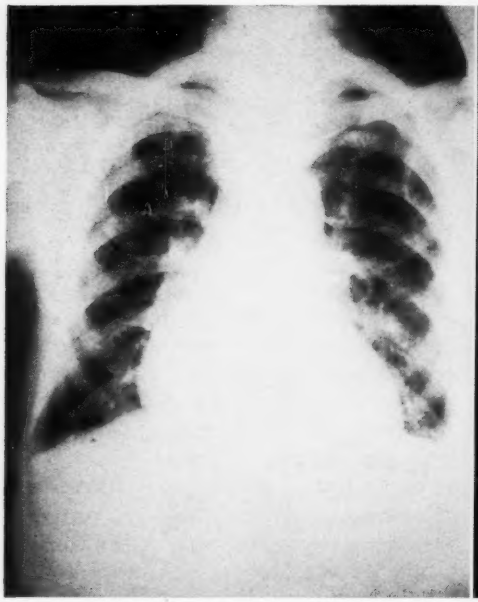

Fig. 3.

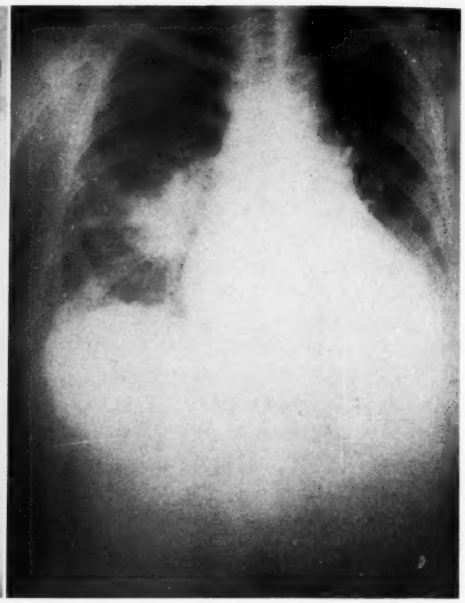

Fig. 4.

Fig. 3. Roentgenogram showing Grade II visibility of right horizontal fissure with enlargement of cardiac shadow.

Fig. 4. Roentgenogram showing Grade III visibility of right horizontal and oblique fissures due to accumulation of transudate, identified by transverse roentgenography, and disappearance with recovery of cardiac compensation.

This point determined, the question of the mechanism by which the opacity of the fissure was increased appeared important. Conceivably, the incidence of lines in the normal cases may represent the result of the fortuitous tangency of the interlobar pleura to the roentgen rays, a factor presumably constant in the tuberculosis and cardiac series. The 100 per cent increase in incidence of linear shadows in the tuberculosis cases might be due to inflammatory infiltration of the sub-pleural parenchyma of the lung, an inflammatory effusion into the fissure, or a pachypleuritis. The first and last would appear more likely to result in coarse lines, a conjecture compatible with the highest incidence of Grade III

lines in this series of roentgenograms. In the 150 per cent increase over normalcy in the occurrence of lines in the cardiac fifth showed slight generalized pleural effusion.

Twelve autopsies were available in cases

TABLE III

Type of Disease	All Heart Dis. 1933–1938	Line Absent 92 Cases	Line Grade I 103 Cases	Line Grade II 14 Cases	Line Grade III 2 Cases
Rheumatic	34%	14%	20%	14%	100%
Arteriosclerotic	16%	20%	19%	21%	0%
Hypertensive	23%	27%	32%	21%	0%
Syphilitic	3%	26%	18%	36%	0%

This table shows the percentage of occurrence of the principal types of heart disease in general cardiac hospital population, and in absence and grades of presence of lines in chest roentgenograms, corresponding to right superior pulmonary fissure.

cases, inflammatory factors are largely eliminated in favor of hydrostatic ones. This is reflected in the less frequent occurrence of heavy lines than in the tuberculosis series. Yet fluid might accumulate upon either the pulmonary or the fissural side of the pleura. Therefore, the determination of the incidence of frank pleural effusion elsewhere in the right chest and of the usual x-ray appearance of passive congestion appeared important. This analysis is noted in Table II.

The importance of pleural effusion in increasing the visibility of fissures is apparent from this analysis in the ascending incidence of frank effusion in the coarser types of linear shadows. The same observation pertains, in lesser degree, to passive congestion. Roentgenographs showing characteristics of both congestion and effusion were included with the group of effusions. Of the two mechanisms, however, hydrothorax would appear, from a consideration of the data tabulated, to be the more important factor.

This apparent importance of effusive and congestive factors, of proliferative changes in increasing the visibility of the horizontal fissure, and the pathologic significance of such visibility is further borne out by the autopsy material available from the cardiac series. Five autopsies were done on cases with enlarged hearts, but without demonstrable fissural lines in antemortem roentgenographs. Four of these showed entire normalcy of the right pleura and the absence of demonstrable effusion; the which had shown fine lines in antemortem x-rays. Of these, but one was normal, while seven showed right hydrothorax of varying degree and four had interlobar adhesions. Of the two autopsy reports available in material of medium caliber lines, one showed normalcy of the pleura with effusion, and the other both hydrothorax and adhesions. No autopsy was available on Grade III material. Again, therefore, the pathologic significance of pleural lines of even fine caliber is obvious, while the rôle of effusion in the creation of these shadows appears of greatest prominence. The type of heart disease represented in the autopsied cases included all the usually important classes without a significant preponderance of any one group.

It is further interesting to examine the 211 hospital charts, available in the cardiac series of roentgenograms, in terms of the types of heart disease represented. This analysis is made in Table III. Comparison is also made with the incidence of various types of heart disease among the cardiac population of the hospital in the years 1933–1938. The less common types of heart disease and the occasional unclassified cases are omitted because of the statistical insignificance of their numbers. The unusually low incidence of syphilitic heart disease in the general hospital population would appear to be due in part to discrimination in admissions, and, possibly, in part to early faulty classification.

Were the inflammatory factors of predominant importance in rendering fissural

pleuræ visible, as suggested by Starr and Parrish (18), the proportion of rheumatic heart disease to the degenerative types of heart disease in cases showing pleural lines should be relatively higher than in the cases showing no fissural lines. The incidences of rheumatic, arteriosclerotic, hypertensive, and syphilitic types of heart disease, however, were essentially the same in groups with and without the fissural shadows. It appears, therefore, that cardiac enlargement and presumably failure, with resulting effusion and passive congestion, are more important mechanisms in the visibility of pleural lines than any other factor common to a given type of heart disease. The lesser proportion of syphilitic heart disease in the general hospital population than among the group under discussion is possibly the result of factors noted heretofore, while the comparatively low incidence of rheumatic disease among the special groups under study, both with and without lines, is probably due to the large numbers seen before cardiac enlargement was significant, and, therefore, included among the hospital population but not admitted to the present study.

Among the instances of rheumatic disease in the present group, mitral valvular lesions predominated over aortic valvular lesions in the ratio of three to one, in that group demonstrating pleural lines, but occurred in equal numbers in instances in which pleural lines were not demonstrable. Among the mitral valvular lesions, insufficiency appeared in twice as many cases as did stenosis, judging from the clinical appraisal of the heart examination, regardless of the presence or absence of demonstrable x-ray fissural lines. It is thus apparent again that factors favorable to pulmonary congestion or pleural effusion predominate in those cases in which pleural lines are found.

Instances of retrogression of localized interlobar pleural effusions with recovery of cardiac decompensation have been reported (22), the localized accumulations being conditioned as already explained by incomplete obliteration of the pleural space. Such an accumulation is illustrated by Figure 4, in which the density in the right lung-field near the hilus is shown by lateral projection to be due to effusion in the oblique fissure adjacent to, and communicating with, the horizontal fissure, and disappearing with recovery of compensation, resulting in the ultimate disappearance of the line before the patient was discharged from the ward. The rôle of effusion in causing such linear visibility is thus again suggested.

SUMMARY

It would, therefore, appear to be unquestionable that although pleural lines corresponding to the right horizontal fissure, and at times or with special technic, to the oblique fissures of the lung, occur in approximately one-fifth of the normal chest roentgenograms, their 100 per cent greater incidence in cases with right-sided pulmonary tuberculosis, and their 150 per cent greater incidence in cases showing enlarged hearts are significant of their frequent pathologic character. Such pathology might conceivably include infiltration, mechanical congestion, and pleural effusion. It is demonstrated herein that all of these exert a definite influence when present. The predominant rôle of effusion into the pleural fissures with the creation of a film of fluid greater than normal, though still of capillary thickness, is evident, from a consideration of the above data, and this mechanism may be assumed to account for the increased visibility of the interlobar fissures, under the circumstances of the present study.

CONCLUSIONS

1. Lines corresponding to the horizontal fissure of the right lung occur in 20 per cent of normal chest roentgenograms.

2. The incidence of such lines in cases of right-sided pulmonary tuberculosis is 100 per cent greater than normal.

3. The incidence of such lines in cases with cardiac enlargement is 150 per cent greater than normal.

4. The lines of heavy caliber are particularly significant of pathology and rarely occur in otherwise normal chest roentgenograms.

5. The cause of such greater visibility of the horizontal fissure is most often a thickening of the film of interlobar pleural fluid by hydrothorax, of frequently otherwise undetectable degree.

6. Inflammatory pleural and subpleural condensations are occasional factors in increasing the visibility of these pleural lines.

7. Such increased visibility of the fissures occurs in cases with cardiac enlargement independently of the type of heart disease present, but particularly correlated with the degree of decompensation.

8. The significance of fine pleural lines in any given instance must be determined according to the merits of the individual case in view of the 20 per cent incidence of such lines in the series of otherwise normal roentgenograms of the chest.

40 S. Third Street

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AN EXPERIMENTAL STUDY OF THE EFFECTS OF ROENTGEN RAYS ON THE GONADS OF THE SEXUALLY MATURE DOMESTIC FOWL[1]

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WITH the aid of standardized x-ray equipment we have undertaken a systematic study of the effects of roentgen rays on the gonads of the domestic fowl. In this study, we have attempted to correlate the age of the animal, the dosage given, and the results obtained. In the first part of the study (1) we were dealing with the embryo and the young chick. The present paper deals with the study of the adult male and female bird.

MATERIALS AND METHODS

The x-ray machine[2] used was mechanically rectified and provided with a Landauer roentgenometer. A universal Coolidge therapy tube was used. The setup of the machine for the entire experiment was as follows: The kilowatt meter was set at 96, which delivered 112 kv.p. as measured by the sphere gap; the milliammeter was set at 6 ma.; the focal distance was 10 in.; the filter was equivalent to 4 mm. aluminum; the roentgenometer was kept at 3.2 micro-amperes, which, by calculation, gave 0.6 r per second. The desired r, or dosage, was obtained by varying the time of exposure.

Young, sexually mature White and Brown Leghorn hens and roosters were selected for the experiment. The age of the birds varied from eight months to one year. They were securely strapped onto a specially constructed stand with the back of the birds directed toward the target. The irradiation stand was so constructed as to facilitate adjustment of the focal distance for each separate bird.

All of the birds except the roosters of Series One were protected during irradiation by a sheet of lead. An opening 2 in. square was cut in the lead plate and placed directly over the gonad area during exposure to the x-rays. Series One was irradiated without such protection.

Both filtered and unfiltered rays were used in the present experiment. The former proved more effective and gave more steady results; for these reasons filtered rays were used almost exclusively.

Testicular tissue was fixed either in 10 per cent formalin and treated with mercuric acetate, or in Bouin's picric acid solution. The latter fluid proved also very satisfactory for ovarian tissues. The tissues were embedded in paraffin and sectioned from 4 to 10 micra in thickness. Hematoxylin-eosin staining was used.

RESULTS: IRRADIATION OF ROOSTERS

In this experiment, 71 specimens were used. Of these, 10 were controls. The 61 irradiated birds numbered 35 roosters and 26 hens. The experimental results obtained in irradiation of the males will be discussed under the following three topics.

Series One.—Ten roosters were irradiated with one dose of x-rays, ranging from 1,216 to 2,816 r. One week elapsed between irradiation and the time the bird was killed. Although the dorsal gonadal area was placed in direct line with the target the other areas of the body were not protected from the rays. In the lower ranges, namely, from 1,216 to 1,856 r, pycnosis of the nuclei in primary and secondary spermatocytes was the major visible pathology. There was a corresponding decrease in the number of spermatids. Spermatogonia and Sertoli cells seemingly were not affected. Likewise the interstitial tissue and vascular supply showed no alterations (Fig. 1). In the higher doses of this series, that is, from 2,176

[1] Submitted for publication in April, 1939.

[2] Type C model, made by the Standard X-ray Company.

to 2,816 r, pycnosis of the nuclei was accompanied by fragmentation of the cytoplasm. This was seen especially in primary and secondary spermatocytes, spermatids, and in some spermatogonia (Fig. 2). When the spermatids possessed pycnotic nuclei, the spermatozoa were absent in the lumina of the tubules. The interstitial tissue exhib-

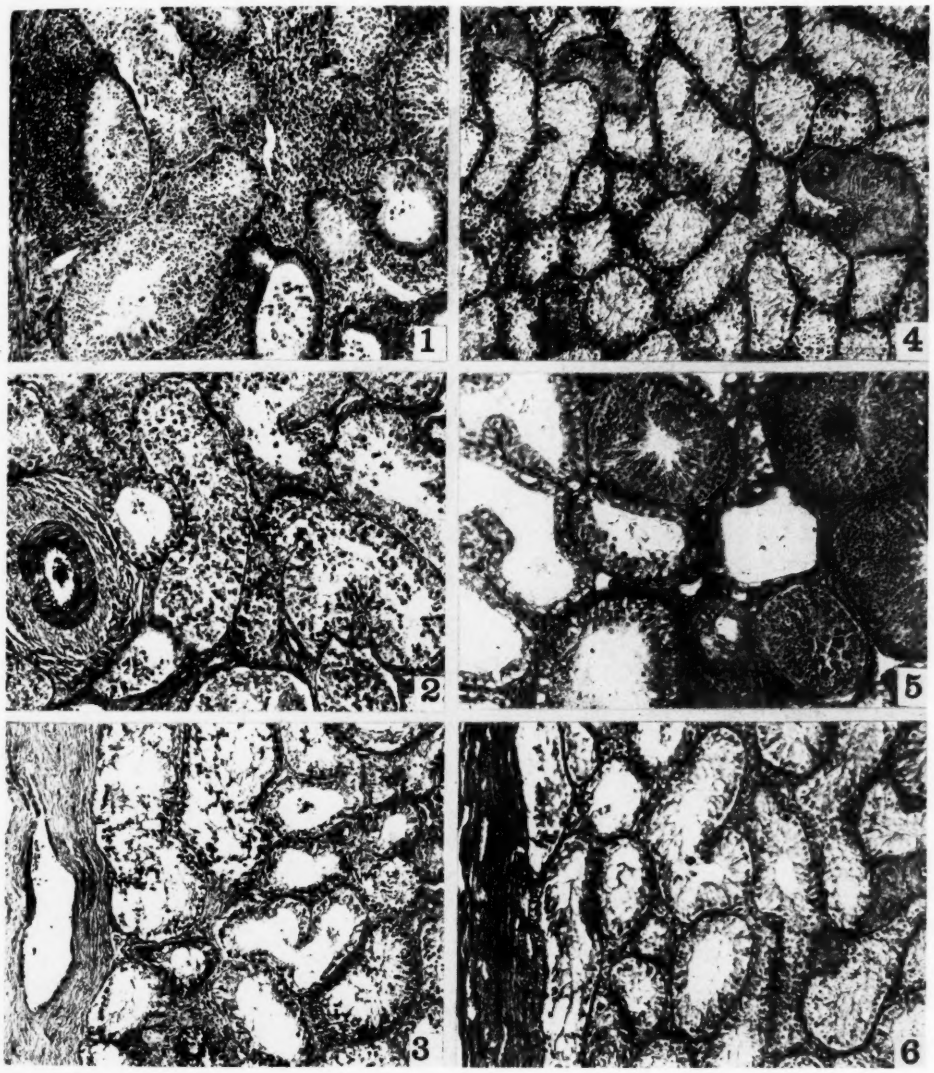

Fig. 1. Section of a testis irradiated with 1,536 r. Apparently normal spermatogenesis occurs in most of the tubules. Note infiltration of lymph cells (× 125).

Fig. 2. Section of a testis treated with 2,496 r. Destruction and exfoliation of seminiferous epithelium; thickening of adventitial coat of arteries (× 125).

Fig. 3. Section of a testis x-rayed with 2,496 r. Destruction of seminiferous epithelium more advanced. Note thickened tunica albuginea (× 125).

Fig. 4. Section of a testis irradiated with 2,496 r. The breaking down of the Sertoli cell and the spermatogonia is shown. The arteries are practically obliterated (× 125).

Fig. 5. Section of a testis treated with a cumulative dosage of 400, 600, and 800 r. "Denuded" tubules occur side by side with tubules with apparently normal spermatogenesis (× 125).

Fig. 6. Section of a testis treated with a cumulative dosage of 1,000, 1,200, and 1,400 r. The destruction is similar to that seen in Figure 4 (× 125).

ited no microscopic changes but there was an increase in the thickness of the adventitial coat of the small arteries. Some evidence of an endarteritis was present in some of these vessels.

Series Two.—Twelve roosters were irradiated with doses ranging from 2,176 to 2,816 r. These specimens were permitted to live three weeks after irradiation. Histologic examination revealed that spermatogonia and Sertoli cells showed a greater resistance to the action of the x-rays. Spermatocytes were, in general, necrotic, also characterized by pycnosis and plasmolysis (Fig. 3). Spermatids as well as spermatozoa were absent in the tubules. The interstitial tissue seemingly was of normal structure. The arterioles exhibited an endarteritis (not obliterative), and a thickening of the tunica adventitia. In all of the specimens of this series the tunica albuginea showed an appreciable increase in thickness. In some instances there was as much as three times the thickness found in the controls. No. 122 of this series (Fig. 4), which received 2,496 r of filtered rays, deserves special mention: in this, the tubules were filled with the broken-down substance of the Sertoli cells, and only a few of the spermatogonia were present. Other findings of this specimen corresponded to those of the other members of this series.

Series Three.—It was composed of 13 roosters. These specimens received three successive doses of x-rays at intervals of one week and were killed three weeks after the last irradiation. The dosage varied from the low combination of 400, 600, and 800 r to the maximum of 1,200, 1,400, and 1,600 r. Histologic sections, viewed macroscopically, presented a mottled appearance. Microscopically the mottling was seen to be due to vastly different changes in adjacent tubules. In many tubules, the seminiferous epithelium consisted of but a single layer of spermatogonia, whereas the neighboring tubules possessed all the layers of normal seminiferous epithelium with an apparently increased mitotic activity and spermatogenesis (Fig. 5). The proportion of "denuded" tubules to unaffected tubules increased as the dosage increased. In specimens having received 1,000 r or more as an initial dose, the seminiferous epithelium was reduced to a single layer of cells, spermatogonia and Sertoli cells. These cells showed definite signs of degeneration (Fig. 6). The adventitia of the arteries and the tunica albuginea of these specimens were much thicker than in the controls. Accumulations of lymph cells were found in practically all of the x-rayed material. No definite alterations could be demonstrated in the interstitial tissue.

IRRADIATION OF HENS

Just as the testes showed structural changes due to irradiation, the ovaries also demonstrated the effects of x-rays. Altogether, 20 hens were subjected to single doses of x-rays. The doses ranged from 400 to 2,176 r and the hens were killed three weeks after irradiation. The mortality rate was very high in the specimens treated with 1,856 r or more and, therefore, only five specimens are present in this lethal dosage range.

Low Dosage Series.—The specimens irradiated with 400 to 700 r showed initial injury to the ovary which was evidenced by the shrinkage of the nucleus of the ovum (Fig. 7). Extensive follicular degeneration was noted with dosages ranging from 800 to 1,200 r. The yolk of many large follicles was invaded by proliferations of the cells from the stratum granulosum and in some instances by connective tissue from the theca folliculi. The effects of irradiation of small follicles were characterized by the scalloping of the nuclear membrane of the ovum and the atrophy of nuclear and cytoplasmic contents. The germinal epithelium presented considerable variability in the same specimen. In some parts of the ovary it appeared normal in structure, whereas in most parts it consisted of a single layer of flattened cells. Primary follicles were found only in regions of active germinal epithelium. Hemorrhagic areas were found in many parts of the ovary but particularly in the cortex,

where they showed signs of degeneration and absorption. Multinucleated giant cells were abundant in such areas. A variable amount of pigment granules, resembling melanin, was present in the interstices of the cortical tissues. The medullary por-

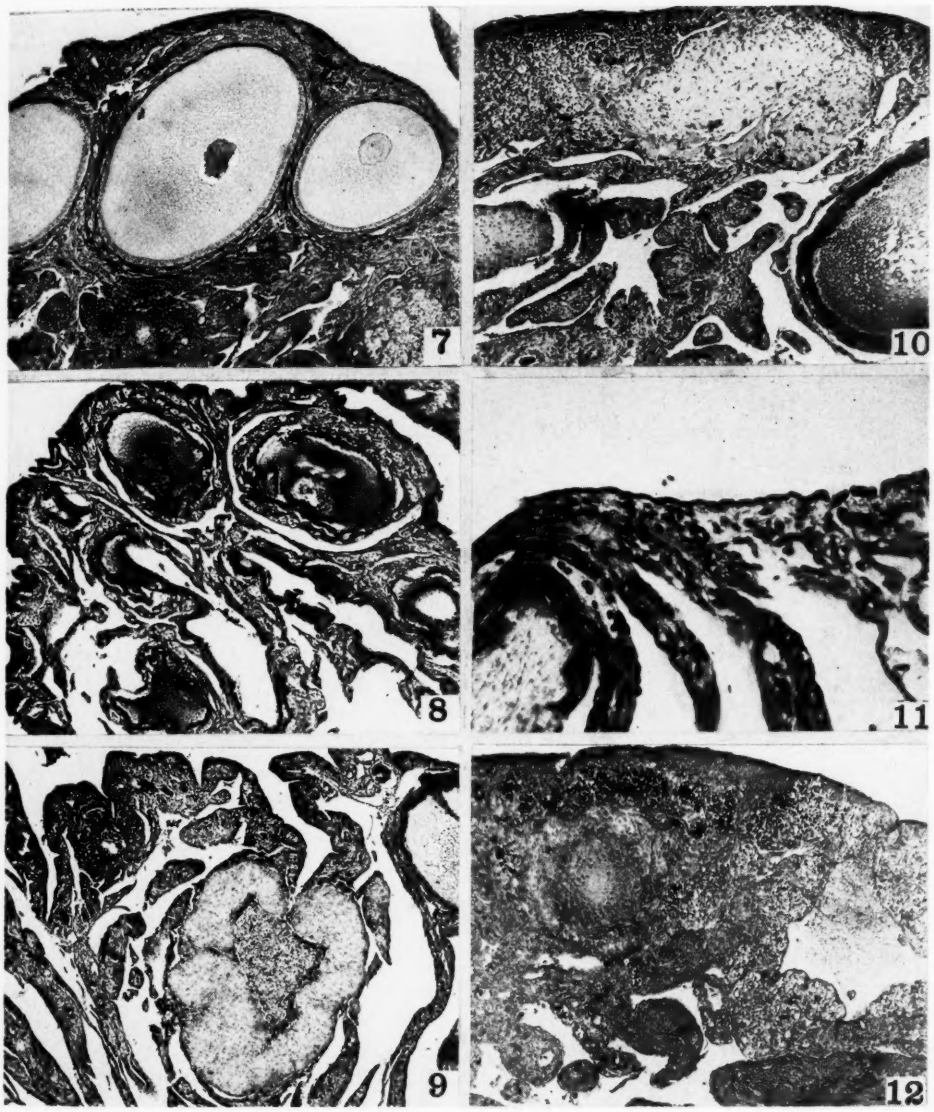

Fig. 7. Section of an ovary showing initial injury caused by 400 r of x-rays. Note the shrinkage of the nucleus and the scalloping of the nuclear membrane (× 83).

Fig. 8. Section of an ovary irradiated with 2,176 r. Note destruction of follicles and germinal epithelium (× 90).

Figs. 9 and 10. Sections from an ovary x-rayed with 2,176 r showing different stages of degeneration of the ovarian follicle (× 420).

Fig. 11. Section of an ovary irradiated with 2,176 r. Note the exfoliation of the germinal epithelium (× 420).

Fig. 12. Section of an ovary treated with a cumulative dose of x-rays. Note the melanin-like pigment granules (× 150).

tion of the ovary presented the least pathology.

High Dosage Series.—The results obtained from hens irradiated with dosages of from 1,200 to 2,176 r differ from those of lower dosages in severity of injuries to the ovary. The follicular degeneration was greater, as indicated by ingrowths of the cellular layer and connective tissue into even the small follicles. The degenerating follicle seldom remained spherical in shape. With the atrophy of the ovular contents the entire follicle collapsed. The most common form of a collapsed follicle was that of a crescent (Fig. 8). Gradually the contents of the follicle, except some of its connective tissue, disappeared entirely (Figs. 9 and 10). The germinal epithelium was more severely affected than in the specimens of the former group. Mitosis was nowhere seen; instead, exfoliation of its cells was taking place in all parts of the ovarian cortex. In many places the ovary was covered by a thin layer of connective tissue (Fig. 11). As would be expected, primary follicles were totally absent from ovaries treated to higher dosages of x-rays. Pigment granules and hemorrhagic areas were noted in the cortex. The thickening of walls of small arteries and the reduction of size of their lumina were found in practically all of the ovaries irradiated. In some instances, the lumina were almost occluded.

Cumulative Dosage Series.—A small series of hens received three consecutive doses of filtered x-rays at intervals of one week. The dosage varied from the low combination of 400, 600, and 800 r to the maximum of 1,200, 1,400, and 1,600 r. The hens were killed three weeks after the last irradiation. The results obtained were fairly uniform in all the specimens of this series. Almost all follicles, large and small, showed degenerative changes. In large follicles, the nuclei were in the last stages of disintegration and the yolk was encroached upon by proliferations of the cellular layer of the follicle, and in some instances by connective tissue. Small follicles invariably possessed scalloped nuclei and in many instances were being obliterated by connective tissue. Primary follicles were not found in any of these specimens. Perhaps the greatest variability in the ovaries of this series was noticeable in the germinal epithelium, particularly in the specimens that had received the low dosage combinations of x-rays. In most parts of the ovary it was reduced to a single layer of flattened cells; rarely it was totally destroyed and exfoliated. In some places what appeared to be an active germinal epithelium was found. The cells were cuboidal in shape with oval or spherical nuclei, and indications of mitosis seemed to be present. However, fully formed germ cells could not be found any more than primary follicles. In the higher dosage series, the germinal epithelium was reduced to a single layer of flattened cells or was totally destroyed and exfoliated. There were no signs of regeneration. In all of the ovaries of this group, hemorrhagic areas containing multinucleated giant cells were found. A variable amount of pigment, morphologically similar to that described in a series treated with a single dose of x-rays, was present in the stroma of the cortex (Fig. 12). The medulla of these ovaries showed increase of fibrous connective tissue, and the arterioles had thickened walls and small, sometimes almost occluded, lumina.

DISCUSSION

With few exceptions the results of the present experiment parallel the results of the first study in which embryos and young chicks formed the material (1). One of the major exceptions of this experiment consists in the absence of cell-cord formation in the ovaries injured by x-rays; growing and fully formed ovarian follicles degenerate completely, primary follicles, very likely, follow the same fate, although the survival of individual cells of the broken-down follicle is not excluded. Another of the major exceptions is that no increase of interstitial tissue has been noted in the present experiment. The dosage required for initial injury was

higher in this than in the former experiment. The testes proved to be more resistant to x-rays as in the former experiment.

An x-ray dosage of 1,200 r was required to produce initial injuries to the seminiferous epithelium of the adult male bird. The first cells injured were the rapidly multiplying primary spermatocytes and next the secondary spermatocytes. The spermatogonia, spermatids, and Sertoli cells seemed to be affected the least. Similar observations have been made in rats and guinea pigs (2). In the more severely affected seminiferous tubules, there was a total lack of primary and secondary spermatocytes; yet, the transformation of spermatids into spermatogonia appeared undisturbed as far as the microscope could reveal. The injuries produced by 1,200 or more units of x-ray varied with different animals and with different levels of the same seminiferous tubule.

The first of the so-called denuded seminiferous tubules occurred in testes treated with dosages of about 2,000 r. In such tubules all of the seminiferous epithelium has been destroyed except the spermatogonia and the Sertoli cells. The cellular débris has been discharged or absorbed and the tubules appear empty in sectional views. The number of such denuded tubules varied with the dosage used; in testes treated with 2,400 to 2,800 r, practically all the seminiferous tubules were denuded. The spermatogonia and Sertoli cells that remained attached to the basement membrane of the tubule were few in number and abnormal in appearance. It seems likely that with higher dosages, all of the seminiferous epithelium is permanently destroyed. This conviction is supported by the findings in the specimens killed three weeks after irradiation when there was ample time for recovery. The increased amount of connective tissue in the tunica albuginea and the adventitia of the arteries seems to indicate stimulating effect of x-rays on supporting tissues.

In the cumulative series, the denuded tubules varied with the total dosage. There were few of the denuded tubules with 1,800 r, more with 3,600 r, but with the total dosage of 4,200 r they were the only tubules present. The histologic structures of the seminiferous tubules, tunica albuginea, and the arterial coats of the high cumulative dosages are identical with the same structures of the testes which received a high (2,800 r) single dose of x-rays. It is clear that considerable acclimatization has taken place in cumulative irradiation. The occurrence of a denuded portion of tubules aside from those with normal spermatogenesis is interpreted as a function of the cyclical activity of the seminiferous tubule. The portions of tubules in a low cyclical phase at the time of irradiation have escaped damage, whereas those in high activity have been destroyed.

The wrinkling or scalloping of the nuclear membrane proved to be the first observable sign of x-ray injury to the ovary. It occurred in all irradiated ovaries, beginning with a dosage of 400 r. Whether or not recovery follows such initial injuries cannot be answered from the histologic observation. X-ray injuries of more serious nature were first noted in specimens irradiated with 800 r, and increased with the increase of the dosage. Most commonly, such follicles collapse into crescent- or star-shaped forms. The collapse is probably due to shrinkage of the nucleus and the yolk. The ingrowing stratum granulosum and theca folliculi seem to assist in the resorption of the follicular contents. After the yolk is removed the cells are large, polyhedral, light-staining structures that have some resemblance to luteal cells of mammals (Fig. 9). Similar structures have been observed in the follicles of x-rayed mice (2, 3, and 4). It is likely that total destruction of the follicular content of the ovary is produced by dosages ranging from 1,800 to 2,200 r.

The total dosage in the cumulative series of hens was as high as in the case of roosters, *i.e.*, from 1,800 to 4,200 r. This is remarkable when it is remembered that the lethal dose of hens was in the neighborhood of 2,200 r, whereas that of roosters was

about 2,900 r. From these data it would appear that the power of acclimatization to x-rays is greater in female than in male birds.

The reaction of the germinal epithelium to the effects of x-ray brings to light some interesting facts. It is effected with dosages as low as 400 r but the effect is not the same in all parts of the ovary. It is reduced at some places to a single layer of flat cells, whereas in other places it consists of several layers of cells in thickness. In the former location there are no signs of mitosis or primary follicles, whereas in the other location both mitosis and primary follicles occur. Mitosis and primary follicles have been noted in specimens treated with a single dose of 1,200 r. Beyond that dosage complete destruction probably results, which is witnessed by cellular exfoliation. The findings are the same with cumulative dosages. It is clear that the germinal epithelium acts in a cyclical manner, the same as the seminiferous epithelium. This conclusion is further strengthened by the fact that in the cumulative dosages the areas of activity decrease as the dosage increases. This observation, as far as the writers know, has not been reported before.

The melanin-like pigment granules were found in both testes and ovaries. They were, however, by far more abundant in the ovaries than in the testes and particularly in the ovaries treated to cumulative dosages. Their sources of origin remain unknown but the frequency at which these granules occur in irradiated ovaries and testes forces the conviction that x-rays are the causative factors.

SUMMARY

In the present experiment 71 young, sexually mature birds were used. Of these there were five male and five female controls, 35 male and 26 female experimental birds. Twenty-two of the 35 males were irradiated with a single dosage ranging from 1,276 to 2,816 r; 13 received three cumulative dosages, the total of which varied from 1,800 to 4,200 r. Twenty of the 26 hens were treated with a single dose, ranging from 400 to 2,176 r, and six were irradiated with three cumulative doses, the total of which varied from 1,800 to 4,200 r. The roosters of Series One were sacrificed one week after irradiation, and the rest of the experimental birds were killed three weeks after treatment. The results are as follows:

(1) With few exceptions the results of the present experiment parallel those of the former study.

(2) A dosage of 1,276 r was required for initial injury and 2,400 to 2,800 r for total destruction of the seminiferous epithelium.

(3) The order of susceptibility of the cells of the seminiferous epithelium to x-rays is: spermatocytes, spermatids, spermatogonia, and Sertoli cells.

(4) X-ray injury to the seminiferous tubule varies with the level of the spermatogenic wave; the injuries are least at levels of least activity and most at levels of active cellular proliferation.

(5) Initial injury to the ovarian follicle was produced by 400 r, follicular disintegration by 800 r, and total destruction of the follicles from 1,800 to 2,200 r.

(6) The destruction of the ovum is aided by the cells of stratum granulosum and theca folliculi.

(7) Initial injury to the germinal epithelium occurs with 400 r, total destruction with 1,200 r.

(8) The fact that areas of total destruction and areas of cellular proliferation occur simultaneously in the same irradiated ovary proves the presence of cyclical activity in the germinal epithelium.

(9) Acclimatization to the effects of cumulative doses of x-rays was noted in both testes and ovaries of treated birds.

(10) Hyperplasia of fibrous connective tissue was noted in the walls of small arteries and medullary stroma of the ovary and in the walls of small arteries and tunica albuginea of testes.

(11) No definite changes due to x-rays could be demonstrated in the interstitial tissue of the gonads of either sex.

(12) A brown melanin-like pigment was

found in variable quantities in the stroma of irradiated ovaries and testes.

(13) The gonads of birds appear to be more resistant to the effects of x-rays than are the gonads of mammals.

(14) Individual variation was much in evidence in the experiment.

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CASE REPORTS

RETOTHEL SARCOMA OF THE STOMACH

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According to Edling (1), in 1914, Ewing proposed the term "reticular-cell sarcoma" for a portion of the group of tumors then being referred to collectively as "lymphosarcoma" and characterized by an origin not from the lymphatic cells of lymphoid tissue but from its reticulum cells.

The term "retotheliosarcoma," applied to the same group of tumors, has been current since it was introduced by Roulet, of Berlin, in 1930, in his description of certain tumors of lymph nodes and of the epipharynx, tonsils, and other sites in the upper respiratory tract. The further usage "retothel" is merely a variant.

With relation to the larger parent group of sarcomas, leaving out the adult and differentiated forms, lymphosarcomas form one member of a chain of which the other two members are spindle-cell sarcomas and round-cell sarcomas (2). Lymphosarcomas are the most numerous and important of the three, so far as sarcomas in the stomach are concerned.

For a critical discussion of the pathology, the reader is referred to the excellent article of Edling (1). The latter says, in summing up: "I have adopted the term proposed by Ewing because it seems to me to define the nature of the growth more accurately than the name of 'lymphosarcoma' which is more commonly employed."

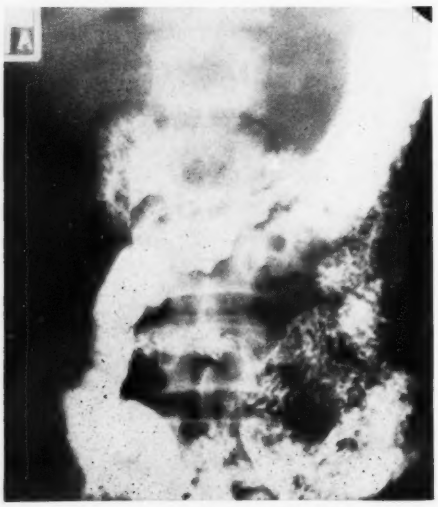

Fig. 1.

The literature contains less than 400 cases of recticular-cell sarcoma of the stomach found at operation and autopsy (3). The lesion was first described by Morgagni, in 1750. Of the cases found at operation, 32 per cent are living after a period of years (3). These figures are not in agreement with those of Haggard, who found a 64 per cent survival after a period of years.

Balfour and McCann reported the operability of the lesions as being 66 per cent of the cases explored.

The youngest patient to have a reticular-cell sarcoma of the stomach was three and one-half years of age (3).

The relative incidence of this lesion, as compared to carcinoma, is usually estimated at about 1 per cent (5). Balfour and McCann found it to vary from 1:56 to 1:226 (6).

Since the constantly changing pathologic concept of the lymphoblastomas brings with recurring insistence a consideration of the blood picture, it may be stated that so far as lymphosarcoma (or reticular-cell sarcoma, or retotheliosarcoma or retothel sarcoma) is concerned, there is nothing constant about the blood picture. Wiseman (7) concludes that "lymphosarcoma is a disease in which there is a transformation of the lymphocytic strain of cells . . . it may show a secondary anemia, or a leukemic or sub-leukemic blood picture."

When the latter is pronounced, the term "leukosarcoma" is frequently employed. Lymphosarcoma may exist in the presence of a full-blown leukemia (13).

The clinical appraisal of sarcoma of the stomach does not extend very far back into our surgical records. As late as 1910, Aimé Guinard (4) questioned the malignancy of sarcoma of the stomach and classed it doubtfully in a group of benign tumors in his *Grand Traité de Chirurgie.*

There is nothing constant about the symptomatology of this lesion. It has been linked with a history of trauma by a few (8 and 9). In Clar's case, the patient, a man 22 years of age, was knocked to the pavement by an automobile, most of the force of the blow being received in the epigastrium. Five months later he was admitted to the hospital with stomach complaints, and after an x-ray examination had shown a filling defect diagnosed as carcinoma, operation revealed a lymphosarcoma.

Jones and Carmody (9) tell of a boy, nine years of age, who was struck in the abdomen by a baseball. His stomach symptoms developed following this injury, and a lymphosarcoma was found at operation. Following resection, the authors obtained a permanent cure (19 years). These writers are impressed by the number of five-year cures they have discovered, and believe that, in selected cases, surgery gives an excellent prognosis.

Others (2) have been struck with the response of the lesion to x-ray therapy.

One case has been reported with a duration of five years before coming to operation (10), in which the clinical symptoms strongly suggested duodenal ulcer. In this case, incidentally, the x-ray examination was relatively negative. Hunt operated upon a case occurring in a child of three and one-half years, who had pyloric obstruction and a mass; post-operative recovery appeared to be complete (3).

Stomach symptoms may be altogether absent (11) and there may be only intense anemia, optic neuritis, and wasting.

The roentgenogram is not in the least diagnostic, so far as naming the lesion to be lymphosarcoma is concerned. There is usually a filling defect in the stomach, which, for obvious reasons, is going to be diagnosed carcinoma.

Golden (12) believes that if there is anything constant about the roentgenogram, it may be a filling defect in which an ulcer crater is made out: this in a young person might lead to a suspicion of sarcoma.

Our patient was a male, A. K., aged 32, of Polish descent. For five months before his admission to Cook County Hospital he had been complaining of a dull, epigastric pain, having no relation to food and shifting once in a while to the left loin. The pain usually came on in the forenoon and lasted for a few hours. It was not severe, and was of an aching character. For two to three days at a time he would have complete relief from the pain; later in the course of the disease it became unremitting.

He had never vomited; he had lost about twenty pounds in weight.

His gastric analysis showed no free acid, combined 9, total 9; there was a small amount of blood and mucus present. Subsequent examinations showed large amounts of blood several times.

Non-protein nitrogen was 33; serum amylase was 60; Wassermann, negative. Blood picture showed hemoglobin, 70 per cent; red blood cells, 4,410,000; white blood cells, 5,500; polymorphonuclears, 66 per cent; lymphocytes, 24 per cent; monocytes, 8 per cent; basophils, 0; eosinophiles, 2 per cent.

On admission, and as a preliminary diagnosis, acute diverticulitis of the colon and acute pancreatitis were considered; hydronephrosis was also considered.

The patient was sent for x-ray examination of the gastro-intestinal tract. Fluoroscopically, and on films, there was a large irregular filling defect, involving both the pars media and pars pylorica of the stomach, which was reported as follows: "Infiltration of the pars media and pars pylorica of the stomach characteristic of an advanced neoplastic process."

Though the films hardly suggested resectability, it was decided to give the patient the benefit of an exploration; this was done on Dec. 17, 1938.

The description of the gross pathology by the surgeon was as follows: "There is a hard mass on the greater curvature of the stomach near the pars media surrounded by massive hard glands and many glands are in the peritoneum and omentum. Five hundred cubic centimeters of peritoneal fluid were removed."

Nothing could be done surgically and the incision was closed. Later, the patient was sent for x-ray therapy, which he received until the time of his death, Jan. 6, 1939.

A gland near the stomach was removed at operation, and the biopsy report is as follows: "Biopsy of lymph node reveals an active retothel sarcoma."

SUMMARY

A case of retothel sarcoma of the stomach is reported, having the following characteristics:

1. The upper abdominal pain of which the patient complained suggested particularly neither ulcer nor carcinoma; on the contrary the tentative working diagnosis included diverticulitis of the colon, pancreatitis, and hydronephrosis.
2. Results of Ewald meal were similar to those in carcinoma.
3. The roentgen appearance of the stomach after barium meal most suggested carcinoma.
4. The patient lived approximately six months after the appearance of his first symptoms.

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MULTIPLE MYELOMA[1]

A CASE REPORT

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The average duration of multiple myeloma is usually given as two years. In a recent survey of 40 cases seen at the University of Michigan Hospital the average duration was two and one-half years. Geschickter and Copeland have stated that the longest duration of any proved case on record was five and one-half years (1). This case was reported by Geschickter in 1930 (2). Subsequent follow-up studies showed that this patient lived approximately seven years after the onset of symptoms (3). The following case is reported because of the unusually long duration of the disease.

R. O., a 49-year-old Jewish female, entered the University Hospital Sept. 27, 1928, complaining of pain in the left hip. This pain had its onset with a fall on the left hip five years previously. The patient had been able to do her work in spite of the pain and an associated limp. The pain was brought on by walking or sitting, and relieved by lying down. One year after the onset of the pain in the hip the patient had noted pain in the anterior aspect of both legs, the spine, and the right shoulder. The use of crutches had been necessary during the three months previous to admission, because walking produced severe suffering. There were no constitutional symptoms except a 26-pound weight loss over a period of four years.

Physical examination revealed a slightly obese, white female, aged 49 years, in fair general health. There was an umbilical hernia. The spine was negative. There was diffuse tenderness over the left hip, pain on motion, and definite limitation of motion. There was diffuse tenderness about the left knee which was otherwise negative. There were bilateral varicose veins of the lower extremities.

Laboratory examination revealed a hemoglobin determination of 70 per cent, 4,050,000 red blood cells per cu. mm., 6,000 white blood cells per cu. mm., and the differential count was normal. Urine examination was negative except for an occasional white blood cell in the sediment. The test for Bence-Jones protein in the urine was negative.

X-ray examination of the pelvis and both hips showed multiple areas of decreased density in the lower half of the left ilium. These areas of decreased density were bounded by lines of increased density, which gave the lesions a trabeculated appearance. The lateral outline of the ilium was irregular, although the cortex was unbroken. There was diminution of joint space in the left hip, with irregularity in the outline of the acetabulum. In the proximal fourth of the shaft of the femur there were multiple oval areas of decreased density similar to those seen in the ilium. Along the lower margin of the femoral neck there appeared to be an area of periosteal bone proliferation. Figure 1 shows the x-ray changes described above. X-rays of the skull and chest were negative.

On Oct. 20, 1928, a biopsy was performed by Dr. Hugh Cabot. Exploration revealed a distinct tumor mass above the left trochanter. The tumor was very soft in consistency, and, when cut, bled furiously. A portion of the tumor was scooped out for pathologic examination. It was noted that there were thin partitions of bone running through the tumor. The bleeding was controlled by packing and partial closure of the wound.

Pathologic examination revealed a myeloma of the plasma-cell type. Figure 2 shows that the individual cells occur in solid sheets, have an eccentric nucleus about half the diameter of the cell, have an abundant eosinophilic cytoplasm, and that within the nucleus there is a spoke-like arrangement of the chromatin. There is practically no intercellular substance.

The biopsy wound healed without incident. On Nov. 6 and 7, 1928, x-ray therapy was administered, 300 r (H.V.L. = 0.9 mm. Cu) being delivered through each of three 20 × 20 ports, over the area of the left hip. This resulted in marked symptomatic improvement, the pain was definitely diminished, and the patient was

[1] Submitted for publication in June, 1939.

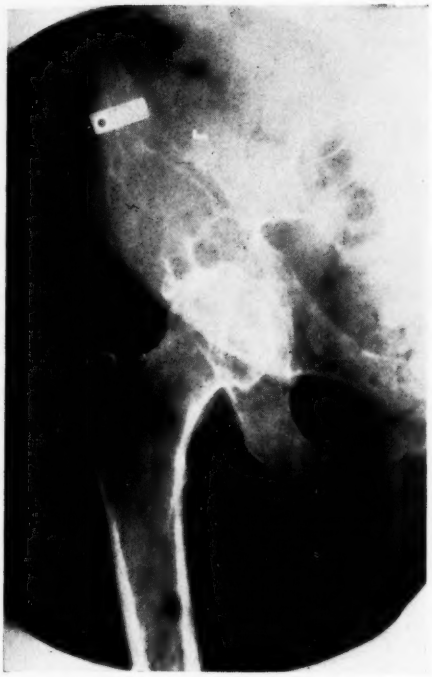

Fig. 1. The x-ray findings on admission showing the areas of destruction in the ilium and upper end of the femur.

able to resume walking. Following the first x-ray treatment similar exposures using 200 r per port were repeated on the average of once per month for the following five months, each time with a favorable symptomatic response.

On Sept. 7, 1929, the patient returned, complaining of considerable pain in the left thigh and spine, and vague pains in the chest. X-ray examination showed regression in the tumor of the left ilium, as evidenced by increased sclerosis in and about the tumor. However, there was evidence of marked dissemination of the malignant process, involving the dorsal and lumbar spine, the ribs, and the shaft and lower end of the right femur. X-ray therapy was repeated to the left pelvis and thigh, and was also administered to the spine, again with symptomatic improvement. The patient was last seen at the University Hospital on Nov. 1, 1930, when she received treatment of 150 r to one port over the left side of the pelvis.

In 1931, the patient was admitted to the Victoria Hospital, London, Canada, on the service of Dr. Stuart Fisher, complaining of recurrence of her original symptoms, with inability to walk. The patient's general condition at that time was excellent.

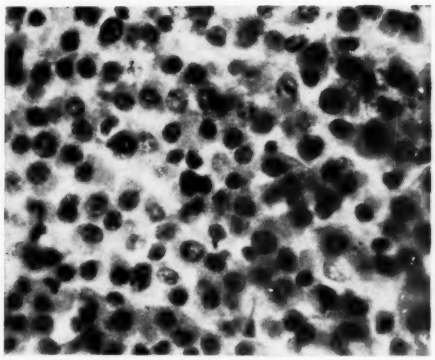

Fig. 2. A high-power photomicrograph showing the characteristics of a plasmacytoma. The cells occur in solid sheets with no visible intercellular stroma. There is an eccentric nucleus, abundant eosinophilic cytoplasm, and many of the cells show a spoke-like arrangement of the chromatin within the nucleus.

In June, 1933, the patient suffered a pathologic fracture of the neck of the right humerus, which was treated, and union resulted. Bence-Jones protein in the urine was first discovered in August, 1933. In 1934, a biopsy of the left fifth rib showed multiple myeloma. From that time until February, 1938, the patient's course was gradually downhill. X-ray therapy was given repeatedly, always with symptomatic improvement. In January, 1938, the skull was found to be involved. The patient died Feb. 4, 1938, 14 years four months after the onset of symptoms, nine years four months after her first admission. No autopsy was obtained.

Beside the long survival of this patient, there are several other facts of interest. Early in the disease the urine was negative for Bence-Jones protein; later it became positive. The pathologic fracture of the humerus healed. The patient uniformly obtained relief of symptoms with x-ray therapy, which is the usual rule in multiple myeloma. It is believed that x-ray therapy not only relieved this patient's symptoms but that it also increased her survival period. In the series of 40 cases previously mentioned, the average survival following treatment in those cases which were treated by x-radiation was approximately twice as long as in those cases which did not receive x-ray therapy.

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THE MODERN HOSPITAL AND ITS RELATION TO THE PRACTICE OF MEDICINE

During the past twenty or thirty years, there have been rapid and extensive changes in the traditional function of the hospital in its relation to the practice of medicine and the delivery of medical care to the American people.

A much larger portion of sick patients are cared for in the private general hospital to-day than was the case a generation ago. Out of every dollar spent for medical care in this country, approximately twenty-four cents goes to pay a hospital bill, either in private or government hospitals (1). This represents a cost of about 656 million dollars per year, of which 300 millions is provided by taxes, 302 millions by patients' fees, and the remainder by contributions and endowments (2). The costs of hospitalization, as a result of illness, is almost as high as the total cost for private physicians' services during a given year. About 86 per cent of the total families in the United States require the services of a physician in an average year but only 20 per cent of the total have at least one hospital case (3). Less than 50 per cent of all family illnesses are hospitalized, yet the costs for hospitalization alone in these cases equals the entire expenditure for all illnesses of the entire family in an average year (4). Half the family bills for illness goes for hospital care, but in any one year only one person in fifteen has hospital care (5).

The cost of medical care in America, therefore, is very largely a cost for hospital care. That this latter cost is entirely justified, is a matter open to serious question. A number of factors have contributed to the increased use of hospitalization and the consequent increased cost of sickness. Many qualified students of the question declare that there is too much hospitalization, and that many patients subjected to the expensive facilities of the hospital could well be cared for in their own home. Three factors are responsible for this alleged over-hospitalization: doctors have referred their patients to the hospital because it was more convenient for the doctor to render his services there; patients have demanded that they be admitted to the hospital when they could just as easily have been treated in their homes, and hospitals have encouraged the use of their facilities with an occasional disregard of the need of the patient for those facilities.

Whether deliberately or not, current tendencies on the part of hospitals find their keynote in the first recommendation made by the Committee on the Costs of Medical Care. In 1929, the Committee recommended that medical care be furnished by groups, organized around a hospital (6). Thus the hospital becomes the dominant factor in the delivery of medical services. The importance of the traditional family doctor as the prime figure in an adequate health program is obscured in a trend toward institutionalized medicine with the hospital as the central figure.

Steps toward this goal were made when hospitals began the operation of pay clinics and out-patient departments in competition with the private physician's office. Abandoned was the old concept that out-patient services and part-pay clinics should be maintained only in teaching institutions where patients should be used for clinical material. Further steps were taken when the "middle rate" plan was adopted by a number of hospitals, in which patients were admitted on an adjusted fee basis including not only the hospital bill, but the bill for medical care as well. Other hospitals instituted "flat rate" or "all inclusive" plans under which a patient could be admitted to the hospital for diagnostic services and pay a flat fee covering the complete cost for medical services and hospital facilities. Still further and more radical steps were taken when hospitals began the sale of insurance plans which offered as benefits not only the use of the physical facilities of the hospital, but the services of medical specialists as well.

Income from endowments and contributions was sharply curtailed after 1929. The 7,000 hospitals in this country represent a capital investment of more than 3 billion dollars, with about 22 millions added each year for expansion (7) and the interest on these investments plus other fixed charges created a difficult problem in finance. Hospitals began to cast about for some new source of revenue to take the place of decreased endowment income.

Group hospitalization insurance presented

itself as a happy solution for the problem, insofar as hospitals were concerned. Started as an experiment by one hospital in Dallas, in 1927, the idea gained little attention until hospitals began to feel the pinch of depression. Then it began a wide and rapid growth.

Less than 65 per cent of the beds in non-governmental hospitals are normally occupied (8), yet fixed charges remain about the same regardless of the number of occupants. So even if hospital insurance increased the number of patients, the steady annual income from insurance premiums would provide the new and necessary revenue.

If hospitals had stopped with the establishment of insurance plans for hospitalization, there would have been little objection from the medical profession which has guarded so zealously the traditional system of American medicine. But, unfortunately, a number of hospitals went still farther to secure new revenue. Ostensibly operated on a non-profit basis, they began to adopt the rôle of a middle-man in the delivery of certain medical services to realize a profit on the services of physicians. Out-patient clinics for pay patients began to grow. Hospitals began to compete with private physicians' offices. Pathologists and radiologists working in the hospital found themselves competing with themselves in their private offices and with their colleagues. Frequently the department of radiology or pathology was operated in such a manner that a large portion of the fees patients paid for these medical services were diverted into the hospital treasury to meet the interest on building investments and other charges.

Here marks a radical departure in the former position of the private non-profit hospital in the medical picture. Doctors had always regarded the hospital as a specially equipped hotel where patients, who could not be satisfactorily treated in their own homes, could be hospitalized. Now the hospital was beginning an invasion of the medical field, and assuming the position of a commercial entrepreneur by interjecting itself between a doctor and his patient, demanding its portion of the fees passing between the patient and his doctor. Many hospitals collected premiums under insurance contracts providing not only hospitalization but the services of physician, radiologist, and pathologist as well.

So the lines of difference were clearly drawn. The medical profession has come to the realization that further encroachments on all types of medical practice are almost sure to follow unless hospitals can be prevailed upon to abandon this unfortunate course, return to the business of hospitalization, and leave the practice of medicine to private physicians.

The medical profession has long maintained that the institutionalization of medical practice or the application of the principles of socialization would result in a lowering of the quality of medical care available to the American people. Taking cognizance of the gradual trend toward such a condition through encroachment of hospitals upon the field of private medical practice, the Judicial Council of the American Medical Association at the annual meeting in 1936, issued a strong statement to the effect that:

"... It would seem that in this time of extensive changes in hospital economics the point had arrived at which further marriages between hospitals and staff physicians that make the doctor of medicine the servant of the hospital should be stopped and a series of attempts at divorce among marriages that have already taken place should be instituted. Our accepted ethical principles are adequate at the present time and hospitals would be of invaluable assistance. It is not an impossible task but will need a militant local and national ethical spirit behind it and a frowning on those individuals in the profession who on personal grounds do not object to the gradual subjugation of the medical profession in the growth of hospital domination" (9).

The Code of Ethics of the A.M.A. provides that:

"It is unprofessional for a physician to dispose of his professional attainments or services to any lay body, organization, group of individuals, by whatever name called, or however organized, under terms or conditions which permit a direct profit from the fees, salary, or compensation received to accrue to the lay body or individual employing him. Such a procedure is beneath the dignity of professional practice, is unfair competition with the profession at large, is harmful alike to the profession of medicine and the welfare of the people, and is against sound public policy" (10).

In this manner the conflicting viewpoints of the medical profession and the hospital group are defined.

The fears of the medical profession in this regard are fully justified by recent statements appearing in hospital publications. These statements evidence a complete disregard of the desires and recommendations of the medical profession. Repeatedly, statements have appeared that hospital service includes radiologic, anesthesiologic, and laboratory services; that the hospital depends upon the profits from the operation of certain medical departments to

maintain the hospital and to increase its income; that the services of the clinician, the surgeon, the pathologist, and the radiologist, as well as the nurse, are a part of the hospital and are services to be provided by the hospital, free from the dictation of medical men.

Practically all States in the Union have enacted statutes prohibiting the practice of medicine by corporations. Similar statutes prevail prohibiting the corporate practice of law, dentistry, and other learned professions. These laws have been passed for the simple reason that the practice of the learned professions by artificial legal entities would not be to the best interest or welfare of the people. Hospital corporations are artificial entities and it is hard to understand why the same reasoning should not be applied in their case. The public would surely suffer as the result of this kind of corporate practice the same as it would in the case of non-hospital corporations. The type of organization is relatively immaterial. In any case, the traditional and indispensable personal relationship between a doctor and his patient will be destroyed or injured under such conditions.

It is true that the authority of the common law is not clear upon the question of the corporate practice of medicine by hospitals. Although important decisions have been rendered by the Supreme Court in several States upholding the statute prohibiting corporate practice, there seems to be a universal reluctance to apply such rulings to hospital corporations. The law, however, has traditionally lagged at least a generation behind the sciences, and the question involved here is a scientific and not a legal one. The important point to consider is whether or not the science of medicine will be preserved and advanced. The general opinion among medical men is that corporate practice, either by hospitals or any other kind of corporation, will hinder the progress of the science and practice of medicine.

The medical profession has found it necessary to wage a militant battle against various forces which have, during recent years, attempted to override the opinion of medical men and bring about revolutionary changes in the form of medical practice in America. In the past, the medical profession has looked upon the hospital as its partner and ally in a relentless fight to preserve the practice of medicine from prejudicial influences.

It will be a great misfortune if the unselfish demands of the medical profession, standing on a firm realization of idealistic principles and scientific truths, be disregarded by a former ally and friend and the hospital shall be found on the side of those dangerous agencies which would substitute their opinions, regarding matters of health, for the opinions of the doctor.

The threat of hospitals in invading the field of medicine, upsetting the traditional relationships between physician and patient, and supplanting free private enterprise with regimented institutionalization is no less than the threat of other radical forces which the hospitals themselves have denounced.

MAC F. CAHAL
Executive Secretary

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(10) Principles of Medical Ethics, p. 20. American Medical Association, Chicago, 1937.

RADIOLOGICAL SOCIETIES IN THE UNITED STATES

Editor's Note.—Will secretaries of societies please cooperate with the Editor by supplying him with information for this section? Please send such information to Leon J. Menville, M.D., 1201 Maison Blanche Bldg., New Orleans, La.

CALIFORNIA

California Medical Association, Section on Radiology.—Chairman, Karl M. Bonoff, M.D., 1930 Wilshire Blvd., Los Angeles; *Secretary,* Carl D. Benninghoven, M.D., 95 S. El Camino Real, San Mateo.

Los Angeles County Medical Association, Radiological Section.—President, M. L. Pindell, M.D.; *Vice-president,* Richard T. Taylor, M.D.; *Secretary,* Wilbur Bailey, M.D., 2007 Wilshire Blvd.; *Treasurer,* Henry Snure, M.D., 1414 South Hope Street; Kenneth Davis, M.D., *Member of Executive Committee.* Meets second Wednesday of each month at County Society Building.

Pacific Roentgen Club.—Chairman, Karl M. Bonoff, M.D., Los Angeles; *Members of Executive Committee,* I. S. Ingber, M.D., A. C. Siefert, M.D., D. R. MacColl, M.D.; *Secretary-Treasurer,* L. Henry Garland, M.D., 450 Sutter St., San Francisco. Executive Committee meets quarterly; Club meets annually during annual session of the California Medical Association.

San Francisco Radiological Society.—Secretary, L. H. Garland, M.D., 450 Sutter Street. Meets monthly on first Monday at 7:45 P.M., alternately at Toland Hall and Lane Hall.

COLORADO

Denver Radiological Club.—President, N. B. Newcomer, M.D., 306 Republic Bldg.; *Vice-president,* Elizabeth Newcomer, M.D.; *Secretary,* Paul R. Weeks, M.D., 520 Republic Bldg.; *Treasurer,* L. G. Crosby, M.D., 366 Metropolitan Bldg. Meets third Friday of each month at homes of members.

CONNECTICUT

Connecticut State Medical Society, Section on Radiology.—Chairman, Samuel M. Atkins, M.D., 63 Central Ave., Waterbury; *Secretary-Treasurer,* Max Climan, M.D., 242 Trumbull St., Hartford. Meetings twice annually in May and September.

DELAWARE

Affiliated with Philadelphia Roentgen Ray Society.

FLORIDA

Florida Radiological Society.—President, H. B. McEuen, M.D., Jacksonville; *Vice-president,* Joseph H. Lucinian, M.D., Miami; *Secretary-Treasurer,* John N. Moore, M.D., 210 Professional Bldg., Ocala. Meetings held in November and at the annual meeting of the Medical Association of Florida in the spring.

GEORGIA

Georgia Radiological Society.—President, James J. Clark, M.D., Doctors Bldg., Atlanta; *Vice-president,* L. P. Holmes, M.D., University Hospital, Augusta; *Secretary-Treasurer,* Robert C. Pendergrass, M.D., Prather Clinic, Americus. Meetings twice annually, in November and at the annual meeting of the Medical Association of Georgia in the spring.

ILLINOIS

Chicago Roentgen Society.—President, Roe J. Maier, M.D.; *Vice-president,* Adolph Hartung, M.D.; *Secretary,* Chester J. Challenger, M.D., 3117 Logan Blvd. Meetings the second Thursday of each month from October to May, except December, at the Hotel Sherman.

Illinois Radiological Society.—President, Harry Ackerman, M.D., 321 W. State St., Rockford; *Vice-president,* D. R. Hanley, M.D., St. Mary's Hospital, Streator; *Secretary-Treasurer,* William DeHollander, M.D., St. John's Hospital, Springfield. Meetings quarterly by announcement.

Illinois State Medical Society, Section on Radiology.—The next meeting will be in Peoria, May 21–23, 1940. The officers are: *Chairman,* Warren W. Furey, M.D., 6844 Oglesby Ave., Chicago; *Secretary,* Harry W. Ackeman, M.D., 321 W. State St., Rockford.

INDIANA

The Indiana Roentgen Society.—President, Juan Rodriguez, M.D., 2902 Fairfield Ave., Fort Wayne; *President-elect,* H. H. Inlow, M.D., Shelbyville; *Vice-president,* Wemple Dodds, M.D., Crawfordsville; *Secretary-Treasurer,* Clifford C. Taylor, M.D., 23 E. Ohio St., Indianapolis. Annual meeting in May.

IOWA

The Iowa X-ray Club.—Holds luncheon and business meeting during annual session of Iowa State Medical Society.

KENTUCKY

Kentucky Radiological Society.—President, D. B. Harding, M.D., Lexington; *Vice-president,* I. T. Fugate, M.D., Louisville; *Secretary-Treasurer,* Joseph C. Bell, M.D., 402 Heyburn Bldg., Louisville. Meeting annually in Louisville, third Sunday afternoon in April.

MAINE

See New England Roentgen Ray Society.

MARYLAND

Baltimore City Medical Society, Radiological Section.—Chairman, Harold E. Wright, M.D., 101 W. Read St.; *Secretary,* Walter L. Kilby, M.D., 101 W. Read St. Meetings are held the third Tuesday of each month.

MASSACHUSETTS

See New England Roentgen Ray Society.

MICHIGAN

Detroit X-ray and Radium Society.—President, Sam W. Donaldson, M.D., 326 N. Ingalls St., Ann Arbor; *Vice-president,* Clarence Hufford, M.D., 421 Michigan Ave., Toledo, Ohio; *Secretary-Treasurer,* E. R. Witwer, M.D., Harper Hospital, Detroit. Meetings first Thursday of each month from October to May, inclusive, at Wayne County Medical Society club rooms, 4421 Woodward Ave.

Michigan Association of Roentgenologists.—President, C. K. Hasley, M.D., 1429 David Whitney Bldg., Detroit; *Vice-president,* M. R. Cooley, M.D., Mercy Hospital, Jackson; *Secretary-Treasurer,* C. S. Davenport, M.D., 609 Carey St., Lansing. Meetings quarterly by announcement.

MINNESOTA

Minnesota Radiological Society.—President, Leo G. Rigler, M.D., University Hospital, Minneapolis; *Vice-president,* Harry M. Weber, M.D., Mayo Clinic, Rochester; *Secretary,* John P. Medelman, M.D., 572 Lowry Medical Arts Bldg., St. Paul. Meetings quarterly.

MISSOURI

The Kansas City Radiological Society.—President, L. G. Allen, M.D., 907 N. 7th St., Kansas City, Kansas; *Secretary,* Ira H. Lockwood, M.D., 306 E. 12th St., Kansas City, Mo. Meetings last Thursday of each month.

The St. Louis Society of Radiologists.—President, Paul C. Schnoebelen, M.D.; *Secretary,* W. K. Mueller, M.D., University Club Bldg. Meets on fourth Wednesday of October, January, March, and May, at a place designated by the president.

NEBRASKA

Nebraska Radiological Society.—President, Roy W. Fouts, M.D., 1007 Medical Arts Bldg., Omaha; *Secretary,* D. Arnold Dowell, M.D., 816 Medical Arts Bldg., Omaha. Meetings first Wednesday of each month at 6 P.M. in Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY

(Maine, New Hampshire, Vermont, Massachusetts, and Rhode Island.) *President,* Langdon T. Thaxter, M.D. Maine General Hospital, Portland, Maine; *Secretary,* Aubrey O. Hampton, M.D., Massachusetts General Hospital, Boston. Meetings third Friday of each month from October to May, inclusive, usually at Boston Medical Library.

NEW HAMPSHIRE

See New England Roentgen Ray Society.

NEW JERSEY

Radiological Society of New Jersey.—President, P. S. Avery, M.D., Middlesex Hospital, New Brunswick; *Vice-president,* J. G. Boyes, M.D., 912 Prospect Ave., Plainfield; *Treasurer,* H. A. Vogel, M.D., 1060 E. Jersey St., Elizabeth; *Secretary,* W. James Marquis, M.D., 198 Clinton Ave., Newark; *Counsellor,* A. W. Pigott, M.D., Skillman. Meetings at Atlantic City at time of State Medical Society, and Midwinter in Newark as called by president.

NEW YORK

Associated Radiologists of New York, Inc.—President, Henry A. Barrett, M.D., 140 East 54th St., New York City; *President-elect,* I. J. Landsman, M.D., 910 Grand Concourse, New York City; *Vice-president,* Frederic E. Elliott, M.D., 122 76th St., Brooklyn; *Treasurer,* Solomon Fineman, M.D., 133 East 58th St., New York City; *Secretary,* William J. Francis, M.D., 210 Fifth Ave., New York City. Regular meetings the first Monday evening of the month in March, May, October, and December.

Brooklyn Roentgen Ray Society.—President, A. L. L. Bell, M.D., Long Island College, Hospital, Henry, Pacific, and Amity Sts.; *Secretary-Treasurer,* L. J. Taormina, M.D., 1093 Gates Ave. Meetings first Tuesday in each month at place designated by president.

Buffalo Radiological Society.—President, Chester D. Moses, M.D., 333 Linwood Ave.; *Vice-president,* Edward C. Koenig, M.D., 100 High St.; *Secretary-Treasurer,* Joseph S. Gian-Franceschi, M.D., 610 Niagara St. Meetings second Monday evening each month, October to May, inclusive.

Central New York Roentgen Ray Society.—President, Jesse Randolph Pawling, M.D., 305 Clinton St., Watertown; *Vice-president,* Albert Lenz, M.D., 613 State St., Schenectady; *Secretary-Treasurer,* Carlton F. Potter, M.D., 425 Waverly Ave., Syracuse. Meetings are held in January, May, and October, as called by Executive Committee.

Long Island Radiological Society.—President, Samuel G. Schenck, M.D., Brooklyn; *Vice-president,* G. Henry Koiransky, M.D., Long Island City; *Secretary,* Marcus Wiener, M.D., 1430 48th St., Brooklyn, *Treasurer,* Louis Goldfarb, M.D., 608 Ocean Ave., Brooklyn. Meetings fourth Thursday evening each month at Kings County Medical Bldg.

New York Roentgen Society.—President, Harry M. Imboden, M.D., 30 W. 59th St., New York City; *Vice-president,* Henry K. Taylor, M.D., 667 Madison Ave., New York City; *Secretary,* Roy D. Duckworth, M.D., 170 Maple Ave., White Plains, N. Y.; *Treasurer,* Eric J. Ryan, M.D., St. Luke's Hospital, New York City.

Rochester Roentgen-ray Society.—Chairman, George H. S. Ramsey, M.D., 277 Alexander St.; *Secretary,* S. C. Davidson, M.D., 277 Alexander St. Meetings at convenience of committee.

NORTH CAROLINA

Radiological Society of North Carolina.—President, Robert P. Noble, M.D., 127 W. Hargett St., Raleigh; *Vice-president,* A. L. Daughtridge, M.D., 144 Coast Line St., Rocky Mount; *Secretary-Treasurer,* Major I. Fleming, M.D., 404 Falls Road, Rocky Mount.

Meetings with State meeting in May, and meeting in October.

OHIO

Cleveland Radiological Society.—President, J. H. West, M.D., 10515 Carnegie Ave.; *Vice-president,* Harry Hauser, M.D., City Hospital; *Secretary-Treasurer,* H. A. Mahrer, M.D., 10515 Carnegie Ave. Meetings at 6:30 P.M. at the Mid-day Club, in the Union Commerce Bldg., on fourth Monday of each month from October to April, inclusive.

Radiological Society of the Academy of Medicine (Cincinnati Roentgenologists).—*President,* Archie Fine, M.D., 707 Race St., Cincinnati; *Secretary-Treasurer,* Justin E. McCarthy, M.D., 707 Race St., Cincinnati, Ohio. Meetings held third Tuesday of each month.

PENNSYLVANIA

Pennsylvania Radiological Society.—President, Louis A. Milkman, M.D., Medical Arts Bldg., Scranton; *First Vice-president,* James E. Ginter, M.D., Dubois; *Second Vice-president,* Alexander Stewart, M.D., Shippensburg; *Secretary-Treasurer,* L. E. Wurster, M.D., 416 Pine St., Williamsport; *President-elect,* Harvey N. Mawhinney, M.D., 6546 Darlington Road, Pittsburgh; *Editor,* William E. Reiley, M.D., Clearfield; *Assistant Editor,* Sydney J. Hawley, M.D., Danville. Next annual meeting to be held May 17 and 18, 1940, at Hershey Hotel, Hershey, Pa.

The Philadelphia Roentgen Ray Society.—President, Joseph E. Roberts, Jr., M.D., 403 Cooper St., Camden, N. J.; *Vice-president,* Jacob H. Vastine, M.D., Medical Arts Bldg., Philadelphia; *Secretary,* Barton R. Young, M.D., Temple University Hospital, Philadelphia; *Treasurer,* Fay K. Alexander, M.D., Chestnut Hill Hospital, Philadelphia. Meetings held first Thursday of each month at 8:15 P.M., from October to May in Thomson Hall, College of Physicians, 21 S. 22nd St., Philadelphia.

The Pittsburgh Roentgen Society.—President, Zoe A. Johnston, M.D., 601 Jenkins Arcade; *Vice-president,* Prentiss A. Brown, M.D., and *Secretary-Treasurer,* Harold W. Jacox, M.D., 4800 Friendship Ave. Meetings held second Wednesday of each month at 4:30 P.M., from October to June at various hospitals designated by program committee.

RHODE ISLAND

See New England Roentgen Ray Society.

SOUTH CAROLINA

South Carolina X-ray Society.—President, Percy D. Hay, Jr., M.D., McLeod Infirmary, Florence; *Secretary-Treasurer,* Hillyer Rudisill, Jr., M.D., Roper Hospital, Charleston. Meetings in Charleston on first Thursday in November, also at time and place of South Carolina State Medical Association.

SOUTH DAKOTA

Meets with Minnesota Radiological Society.

TENNESSEE

Memphis Roentgen Club.—Chairmanship rotates monthly in alphabetical order. Meetings second Tuesday of each month at University Center.

Tennessee Radiological Society.—President, Steve W. Coley, M.D., Methodist Hospital, Memphis; *Vice-president,* Eugene Abercrombie, M.D., 305 Medical Arts Bldg., Knoxville; *Secretary-Treasurer,* Franklin B. Bogart, M.D., 311 Medical Bldg., Chattanooga. Meeting annually with State Medical Society in April.

TEXAS

Texas Radiological Society.—President, C. F. Crain, M.D., Corpus Christi; *President-elect,* M. H. Glover, M.D., Wichita Falls; *First Vice-president,* G. D. Carlson, M.D., Dallas; *Second Vice-president,* P. E. Wigby, M.D., Dallas; *Secretary-Treasurer,* L. W. Baird, M.D., Scott and White Hospital, Temple. Meets annually. The next annual meeting is to be Jan. 18, 1941, in Sherman.

VERMONT

See New England Roentgen Ray Society.

VIRGINIA

Radiological Society of Virginia.—President, Fred M. Hodges, M.D., 100 W. Franklin St., Richmond; *Vice-president,* L. F. Magruder, M.D., Raleigh and College Aves., Norfolk; *Secretary,* V. W. Archer, M.D., University of Virginia Hospital, Charlottesville.

WASHINGTON

Washington State Radiological Society.—President, H. E. Nichols, M.D., Stimson Bldg., Seattle; *Vice-president,* George Cornett, M.D., Yakima; *Secretary-Treasurer,* Kenneth J. Holtz, M.D., American Bank Bldg., Seattle. Meetings fourth Monday of each month at College Club, Seattle.

WISCONSIN

Milwaukee Roentgen Ray Society.—President, H. W. Hefke, M.D.; *Vice-president,* Frederick C. Christensen, M.D.; *Secretary-Treasurer,* Irving I. Cowan, M.D., Mount Sinai Hospital, Milwaukee. Meets monthly on first Friday at the University Club.

Radiological Section of the Wisconsin State Medical Society.—Secretary, Russel F. Wilson, M.D., Beloit Municipal Hospital, Beloit. Two-day annual meeting in May and one day in connection with annual meeting of State Medical Society, in September.

University of Wisconsin Radiological Conference.—Secretary, E. A. Pohle, M.D., 1300 University Ave., Madison, Wis. Meets every Thursday from 4 to 5 P.M., Room 301, Service Memorial Institute.

EDITORIAL

LEON J. MENVILLE, M.D., *Editor* HOWARD P. DOUB, M.D., *Associate Editor*

IS THE PRACTICE OF ROENTGENOLOGY ABOVE CRITICISM?

To one who has practised roentgenology for thirty-three years, it might be permissible to express some observations and, possibly, criticisms of the progress made in this specialty.

During the World War, in the need for roentgenologists, a large number were trained for this purpose. Considering the emergency at that time, they were well trained, but the instruction was insufficient for the private practice of this specialty, which many of these men took up on their return. The value of the x-ray was forcefully demonstrated at that time, with the result that when the War was over and doctors returned to civil practice, they demanded x-ray in their hospitals, even in the smaller towns. This created a demand for a larger number of roentgenologists. As the number of large hospitals (being more or less teaching centers for the universities) increased, another demand was made for more roentgenologists. The training of roentgenologists was begun in the medical courses and, later, special house-officer positions were created for those who intended to enter the specialty of roentgenology, with the result that, in a few years, a large number did enter.

Coming to more recent years, industries have begun to realize the value of medical care of workmen; again an increase in the use of the x-ray occurred. The establishment in various States of Workmen's Compensation Acts added to the need for roentgenology. Furthermore, in the last fifteen years there has been a marked increase in the number of diagnoses and cases of injury resulting from automobile accidents, all of which has increased the amount of work, particularly for the roentgenologist. As we have lived through these various phases of the building up of this specialty, with their marked increase in the use of the x-ray in all phases of civil life, we have been rather appalled at the ease with which diagnoses can be made from the x-ray and yet are so often found to be wrong.

One of the faults of the early German practice of roentgenology, as it came to us as observers, was that the roentgenologist was primarily a trained internist and his interpretations were 90 per cent clinical and 10 per cent x-ray. We do not believe this situation has existed in more recent years in this country, in spite of the gastro-enterologists and the various specialists installing their own equipment for their own purposes. We believe that these specialists who attempt the examination of their own patients by the x-ray cannot help but be biassed by the clinical findings, primarily, and, secondarily, by what the x-ray may show. Perhaps for this reason we are of the opinion that one of the most serious faults of the younger roentgenologist is that, when a case is referred to him, he feels he must make some sort of positive diagnosis in order to retain his consultant. When the case is negative, he is not willing to say so, apparently in fear of the consultant's opinion. Again, if he has had any degree of clinical experience, he is most likely to consider the clinical picture first and that of the x-ray second. One of the great values of the x-ray, it always seems to us, is the lack of bias on the part of the diagnostician, in spite of what the clinical diagnosis might have been or might prove to be. And thus it seems that a negative opinion, a report of a normal condition, or an inability to demonstrate the result of a trauma is as valuable to everyone concerned as a positive diagnosis. We have felt, however, that this was not the opinion of a very large group of roentgenologists.

In the private practice of roentgenology, with some exceptions, it makes little difference if, for example, the roentgenologist calls a change in a vertebra "hypertrophic arthritis" or "hypertrophic change," since the clinician will treat the patient on the basis of the clinical symptoms and not on that of the diagnosis. On the other hand, if the roentgenologist passes an opinion of a fracture, such as a fractured ankle,

and is perhaps wrong in his diagnosis, it makes little difference to the consultant because he will treat the case under the diagnosis and no harm will be done.

When we consider the more complicated compensation work, automobile liability, or accidents in the automotive industry, an accurate and correct diagnosis is of the utmost importance, because, eventually, either in the quasi-court of law or before the higher courts, such diagnoses are evaluated in damages in the form of dollars and cents. The physician who makes either a negative or positive diagnosis of a given condition will be called upon to prove this diagnosis. At the same time, roentgenologists, among others, are called upon to disprove positive diagnoses, and we must have facts which will substantiate our opinion as it differs from that of our colleagues. Mere opinions are not acceptable; one must offer fundamental as well as scientific facts in attempting to prove a positive or negative diagnosis. It is somewhat disturbing in this work to see so many x-ray films, from various parts of the country, submitted by large insurance companies, industries, and railroads, and to find diagnoses which have been made without any basis of fact whatsoever.

An example of this is the fact that, in twenty-one court appearances in one month, we differed eighteen times—practically a difference of 100 per cent—from the original diagnoses. This is rather startling to us because either those who made the positive diagnoses were wrong or we who made the negative diagnoses were wrong. In a careful analysis in a series of cases such as this and with the facts placed before an unbiassed committee of roentgenologists, doubtless there would be 100 per cent agreement on the negative against the positive, or, in this series, at least sixteen cases out of the eighteen. The difference in the other two cases would be academic, for example, the age of a fracture, if it were a fracture case. In analyzing these cases, which we try to do in every instance for our own information and instruction, there appears to be a startling lack of the fundamentals of diagnosis, with no thought of the many varied congenital anomalies of the whole skeleton. If the congenital anomalies are recognized, they are usually recognized as a cause of symptoms in most part, and, if not the cause of symptoms, the possibility of aggravation of symptoms. We believe that a general statement can be made, with few reservations, that none of the congenital anomalies, so commonly and frequently found, is the source of any weakness in structure or symptoms, either by themselves or with accident. Nor do we believe that owing to the defect symptoms are more likely to appear than in the absolutely normal individual.

From the plaintiff's side of the diagnosis, many medico-legal cases are based upon some minor variation. Space will not permit us to cite these, but I will use one, and that is spondylolisthesis. After many years of study, we have come to the firm conviction that, with rare exception, this condition is developmental in origin, possibly from fetal life. When trauma is the cause of this condition, it takes only a few weeks' study of the part to demonstrate definitely by proliferative and reactionary changes that this is the result of the alleged accident.

The second failure of correct interpretation would seem to be a lack of knowledge or interest in whether the change found in the given part is the result of the alleged accident or by its very appearance existed at the time of the accident. This reverts to a rather simple fundamental knowledge of time-element in the production of reactionary changes. Proliferative changes, healing or destructive areas, or calcifications appear and are diagnosed as the result of an alleged injury, in some instances, of from three to five weeks. Here again, when these changes are interpreted as the result of an alleged accident, one can say that there is a fundamental lack of knowledge of the pathologic changes which occur.

Again, when one hears in court the allegation that atrophy in the bones of the shoulder girdle in a well-nourished individual can be demonstrated in the x-ray film in from two days to one week, one feels that roentgenology has progressed rapidly in its ability to demonstrate changes which, to this writer, would seem impossible in this short period of time, much less visible by the x-ray film. In the last analysis, perhaps the x-ray cannot do all we had hoped for it or expected it would; nevertheless, it has its definite place in medicine, and its study is a science of exactness provided we—those of us who interpret—can be exact.

ARIAL W. GEORGE, M.D.

ANNOUNCEMENT

THE NEXT ANNUAL MEETING

The Twenty-sixth Annual Meeting of the Radiological Society of North America will be held at Cleveland, Ohio, in the Hotel Statler, on December 2, 3, 4, 5, and 6, 1940.

COMMUNICATIONS

DR. GEORGE E. PFAHLER HONORED

On Thursday evening, January 25, a testimonial dinner was given Dr. George E. Pfahler by the Philadelphia Roentgen Ray Society at The Warwick, Philadelphia.

Two hundred and fifty friends of Dr. Pfahler came from afar as well as from Philadelphia and its environs.

Dr. Eugene P. Pendergrass was Toastmaster. In the absence of Dr. Joseph E. Roberts, Jr., President of the Society, Dr. Jacob H. Vastine, II, Vice-president, read a message from Dr. Roberts. Other speakers were Dr. Francis F. Borzell, President-elect of the Medical Society of the State of Pennsylvania, Dr. George H. Meeker, Dean of the Graduate School of Medicine of the University of Pennsylvania, and Dr. Joseph McFarland, Professor of Pathology at the University of Pennsylvania. Dr. B. R. Kirklin, Secretary of the American Board of Radiology, read a tribute to Dr. Pfahler written by Dr. Percy Brown, Historian of the American Roentgen Ray Society.

As a memento of the occasion, Dr. W. Edward Chamberlain presented Dr. Pfahler with a silver platter from the Society. Dr. Pfahler accepted the platter with a gracious and modest speech.

The meeting was a pleasant one and this public acknowledgment of the debt which radiology owes Dr. Pfahler, and of the respect and affection in which his confrères and friends hold him, was evident from the large attendance and the remarks which were made.

JOHN T. FARRELL, JR., M.D.

RADIOLOGY wishes to join with those friends of Dr. Pfahler who were permitted to break bread with him, in congratulating him upon his remarkable record in radiology. The Philadelphia Roentgen Ray Society honored itself in honoring him. We like to think over the genial wit and wisdom which must have flowed about that banquet table, at which were gathered the leading exponents of our specialty.

The dinner was attended by Dr. Bernard H. Nichols, President of the Radiological Society of North America, and by Dr. Donald S. Childs, Secretary-Treasurer of that same Society, who expressed the felicitations of our members upon this happy occasion.

Not because of Dr. Pfahler's years of service in the teaching and practice of radiology do we delight to do him honor, but principally because of his ripe scholarship, the wealth of experience which is his, and his helpfulness toward those who have yet to attain their experience. What he has found out for himself he is ready to pass on to others.

RADIOLOGY adds its congratulations, Dr. Pfahler!

MID-WESTERN RADIOLOGISTS' FOURTH ANNUAL CLINICAL CONFERENCE

The Fourth Annual Clinical Conference of Mid-western Radiologists was held at the Brown Hotel, Louisville, Kentucky, on February 9 and 10, 1940. Presentations on many subjects of interest to radiologists were made by some of the leading physicians of Kentucky.

At the dinner meeting Dr. William Allen Pusey, of Chicago, spoke on the subject, "Reminiscences of My Early Experiences with the Roentgen Ray." He presented his office record and case history of the first patient he had ever treated with the roentgen ray, this being done early in the year 1900. He spoke of his therapeutic experiences with the roentgen ray in lesions of many types, many of which were undoubtedly so treated for the first time.

Dr. Irvin Abell, of Louisville, Kentucky, then spoke on the subject, "The Present United States Public Health Program." In prefacing his major presentation he paid a glowing tribute to the radiologist. He spoke of his great importance in the general field of medicine and of the many contributions to medical progress that had been made by radiologists during the last forty years. He also commended radiologists in general for the work that they were doing in preserving their specialty and for their defense against the attempted inroads of so-called Social Legislation. He then gave a remarkable summary of

the legislative activities of our Government in the field of medicine during the past six years, together with a summary of the legislation now before the Congress.

There was a Symposium on the Chest and a Symposium on Carcinoma of the Lung, each comprising five papers, as well as almost thirty papers on various radiologic subjects, presented by leading physicians.

Dr. C. A. Good, of the Mayo Clinic, in behalf of Dr. B. R. Kirklin, invited the Conference to meet in Rochester, Minnesota, next year. The invitation was accepted by the Conference.

THE AMERICAN BOARD OF RADIOLOGY

The next examination to be conducted by The American Board of Radiology will be in New York City, June 7–9, 1940, but the quota is practically filled for this examination. We would, therefore, urge those who are anxious to be examined this year to send their applications in immediately so that they may be scheduled for the examination to be conducted in Boston, Mass., Sept. 27–29, 1940.

Following is a list of those who have been certified or granted additional certification during 1939.

Address all communications to B. R. Kirklin, M.D., Secretary The American Board of Radiology, Mayo Clinic, Rochester, Minnesota.

The following were issued certificates in 1939:

	Name	Address	Field
1.	Abrams, Hyman S.	Tuscaloosa, Ala.	Radiology
2.	Ackermann, Alfred J.	Oklahoma City, Okla.	Roentgenology
3.	Algin, Sergius	Indiana, Pa.	Roentgenology
4.	Allen, William E., Jr.	St. Louis, Mo.	Radiology
5.	Almy, Max A.	Rochester, N. Y.	Roentgenology
6.	Andrew, F. D.	Rochester, N. Y.	Radiology
7.	Ansprenger, Aloys G.	Macomb, Ill.	Radiology
8.	Athle, Laxman H.	Bombay, India	Radiology
9.	Bachman, Arnold L.	Stamford, Conn.	Radiology
10.	Baltimore, Louis	Los Angeles, Cal.	Roentgenology
11.	Barner, John L.	Cincinnati, O.	Therapeutic Radiology
12.	Bayliss, Jacob W.	Buffalo, N. Y.	Roentgenology
13.	Beatty, Samuel R.	Denver, Colo.	Radiology
14.	Bell, Charles E.	East St. Louis, Ill.	Radiology
15.	Bernstein, Alfred J.	New York, N. Y.	Radiology
16	Bersack, Solomon R.	Springfield, Mass.	Radiology
17.	Bond, Thomas B.	Fort Worth, Texas	Roentgenology
18.	Bonis, Alexander	New York, N. Y.	Radiology
19.	Boswell, Frederick P.	Montgomery, Ala.	Radiology
20.	Bracher, George J.	Seattle, Wash.	Diagnostic Roentgenology
21.	Brindle, Harry R.	Asbury Park, N. J.	Roentgenology
22.	Brown, William L., Sr.	Chicago, Ill.	Radium Therapy
23.	Bryan, William W.	Montreal, Canada	Radiology
24.	Bugbee, Edwin P.	Philadelphia, Pa.	Radiology
25.	Burvill-Holmes, E.	Philadelphia, Pa.	Radiology
26.	Butler, William J.	Providence, R. I.	Radiology
27.	Carr, Gladys L.	Hempstead, N. Y.	Roentgenology
28.	Carroll, William J.	Hot Springs, Ark.	Radiology
29.	Casper, Stephen L.	Philadelphia, Pa.	Radiology
30.	Caulk, Ralph M.	Washington, D. C.	Radiology
31.	Chang, C. William	New York, N. Y.	Radiology
32.	Cohen, Paul W.	New York, N. Y.	Therapeutic Radiology
33.	Colton, Benjamin	Flushing, N. Y.	Diagnostic Roentgenology
34.	Conahan, Thomas J.	Hazleton, Pa.	Radiology
35.	Cooney, James P.	Washington, D. C.	Radiology
36.	Cooper, George, Jr.	University, Va	Roentgenology
37.	Cooper, Robert W.	Shreveport, La.	Radiology
38.	Curtzwiler, Francis C.	Toledo, O.	Radiology
39.	Daversa, Joseph J.	Brooklyn, N. Y.	Roentgenology
40.	Dell, J. Maxey	Gainesville, Fla.	Roentgenology
41.	Doble, Eugene H.	Presque Isle, Me.	Diagnostic Roentgenology

42.	Dowdy, Andrew H.	Rochester, N. Y.	Radiology
43.	Echternacht, Arthur P.	Indianapolis, Ind.	Radiology
44.	Elliott, William J.	Worcester, Mass.	Radiology
45.	Epstein, Bernard S.	Brooklyn, N. Y.	Radiology
46.	Euphrat, Edwin J.	Elkins, West Va.	Radiology
47.	Evans, William A., Jr.	Detroit, Mich.	Radiology
48.	Fierstein, Jacob	New York, N. Y.	Roentgenology
49.	Flanagan, E. Latane	Richmond, Va.	Roentgenology
50.	Gartenlaub, Charles	New York, N. Y.	Roentgenology
51.	Gilbert, Philip D.	Camden, N. J.	Radiology
52.	Gilmore, John H.	Chicago, Ill.	Radiology
53.	Good, C. Allen	Rochester, Minn.	Radiology
54.	Grady, Mary Alice	San Francisco, Cal.	Roentgenology
55.	Gray, Charles M.	Tampa, Fla.	Radiology
56.	Grimm, Homer W.	Pittsburgh, Pa.	Radiology
57.	Hall, James B.	Johnstown, Pa.	Roentgenology
58.	Hankins, Walter D.	Johnson City, Tenn.	Roentgenology
59.	Hanley, D. Reed	Streator, Ill.	Roentgenology
60.	Hartung, Walter	Iowa City, Ia.	Radiology
61.	Harwell, Wilbur R.	Shreveport, La.	Radiology
62.	Hayes, Arthur W.	Greenfield, Mass.	Diagnostic Roentgenology
63.	Herrmann, Henry C.	Louisville, Ky.	Therapeutic Radiology
64.	Hiebert, Peter E.	Kansas City, Kans.	Radiology
65.	Hill, John M.	Pittsburgh, Pa.	Radiology
66.	Hilt, Lawrence M.	Grand Rapids, Mich.	Radiology
67.	Hobbs, Arthur A., Jr.	Philadelphia, Pa.	Radiology
68.	Holtz, Harvey E.	Dallas, Tex.	Radiology
69.	Howard, Corbett E.	Goldsboro, N. C.	Therapeutic Radiology
70.	Howe, Martha E.	New York, N. Y.	Therapeutic Radiology
71.	Hummon, Irvin F., Jr.	Oak Park, Ill.	Roentgenology
72.	Hunter, Arthur F.	New York, N. Y.	Roentgenology
73.	Jaffrey, George	Olean, N. Y.	Radiology
74.	Jelte, Safford A.	Oakland, Cal.	Radiology
75.	Jenkins, I. Warner	Waco, Tex.	Radiology
76.	Jenkins, William F.	Columbus, Ga.	Roentgenology
77.	Jensen, Herman H.	Minneapolis, Minn.	Radiology
78.	Jimenez, Juan M. M.	New York, N. Y.	Radiology
79.	Johnson, Roy W.	Los Angeles, Cal.	Radiology
80.	Johnston, Wayne A.	Dubuque, Ia.	Roentgenology
81.	Kelley, Charles H.	Washington, D. C.	Radiology
82.	Kellogg, Douglas S.	Ft. Sam Houston, Tex.	Roentgenology
83.	Kestel, John L.	Waterloo, Ia.	Diagnostic Roentgenology
84.	Kirsh, Israel E.	Salt Lake City, Utah	Radiology
85.	Koenig, Edward C.	Buffalo, N. Y.	Roentgenology
86.	Lake, William F.	Atlanta, Ga.	Roentgenology
87.	Landham, Jackson W.	Atlanta, Ga.	Roentgenology
88.	Larkin, John C., Jr.	Berkeley, Cal.	Radiology
89.	Lavine, Sidney B.	Trenton, N. J.	Diagnostic Roentgenology
90.	Lavner, Gerald	Haverhill, Mass.	Diagnostic Roentgenology
91.	Lawlah, John W.	Chicago, Ill.	Radiology
92.	LeWald, Leon T.	New York, N. Y.	Radiology
93.	Leader, Samuel A.	Lexington, Ky.	Diagnostic Roentgenology
94.	Lerner, Henry H.	Boston, Mass.	Diagnostic Roentgenology
95.	Levy, Abraham H.	Brooklyn, N. Y.	Radiology
96.	Lewis, Elbert K.	Chicago, Ill.	Radiology
97.	Lia, Bianca Rachel	Boston, Mass.	Roentgenology
98.	Liberson, Frank	Brooklyn, N. Y.	Roentgenology
99.	Logan, George E. C.	Philadelphia, Pa.	Radiology
100.	McAlister, Lawrence S.	Muskogee, Okla.	Radiology
101.	McCampbell, Herbert H.	Knoxville, Tenn.	Radiology
102.	McCandless, Oliver H.	Kansas City, Mo.	Roentgenology
103.	McCullough, Thomas L.	Pittsburgh, Pa.	Diagnostic Roentgenology
104.	McGreer, John T.	Dayton, O.	Radiology
105.	McKinney, G. C.	Lake Charles, La.	Roentgenology
106.	McNattin, Robert F.	Chicago, Ill.	Therapeutic Radiology
107.	Mackoy, Frank W.	Milwaukee, Wis.	Diagnostic Roentgenology
108.	Magruder, Levin W.	New Orleans, La.	Radiology
109.	Manley, Louis V.	Northampton, Mass.	Diagnostic Roentgenology
110.	Martineau, Lawrence A.	Providence, R. I.	Roentgenology
111.	Mass, Max	Macon, Ga.	Diagnostic Roentgenology
112.	Maxfield, James R., Jr.	Waco, Texas	Radiology
113.	Meader, Robert P.	Philadelphia, Pa.	Radiology
114.	Mokrohisky, Stephen M.	Green Bay, Wis.	Roentgenology
115.	Moore, J. N.	Ocala, Fla.	Roentgenology
116.	Morgan, Arthur E.	Washington, Pa.	Roentgenology
117.	Morgan, Harold W.	Mason City, Ia.	Radiology

118.	Morris, Clyde L.	Peoria, Ill.	Roentgenology
119.	Myers, Karl J.	Philippi, West Va.	Radiology
120.	Nash, Newman C.	Wichita, Kans.	Radiology
121.	Neely, John M.	Lincoln, Neb.	Radiology
122.	Newton, John O.	Cleveland, O.	Roentgenology
123.	Norton, Richard C.	Battle Creek, Mich.	Diagnostic Roentgenology
124.	Palmer, James P.	Bronx, N. Y.	Radiology
125.	Payne, Andrew K.	Jackson, Mich.	Radiology
126.	Pearlstein, Frank	West New York, N. J.	Diagnostic Roentgenology
127.	Pedersen, Nicholas S.	San Francisco, Cal.	Roentgenology
128.	Phillips, Allan B.	Des Moines, Ia.	Radiology
129.	Piatt, Arnold B.	Tulsa, Okla.	Roentgenology
130.	Plaut, H. F.	Mansfield, O.	Radiology
131.	Pollack, Simon	St. Louis, Mo.	Roentgenology
132.	Popma, Alfred M.	Boise, Idaho	Radiology
133.	Poppel, Maxwell H.	New York, N. Y.	Roentgenology
134.	Prince, Norman C.	Amarillo, Tex.	Roentgenology
135.	Reed, Harold R.	Washington, D. C.	Radiology
136.	Reid, Edward K.	Rome, N. Y.	Diagnostic Roentgenology
137.	Rhinehart, B. A.	Little Rock, Ark.	Roentgenology
138.	Richardson, Maurice L.	Freeport, Ill.	Roentgenology
139.	Roberto, Romeo	Yonkers, N. Y.	Diagnostic Roentgenology
140.	Roberts, Edward W.	Chicago, Ill.	Roentgenology
141.	Robilotti, James G.	New York, N. Y.	Diagnostic Roentgenology
142.	Rodes, Charles B.	Butte, Mont.	Diagnostic Roentgenology
143.	Rogers, Frank T.	Ann Arbor, Mich.	Radiology
144.	Rubin, J. S.	Jamaica, N. Y.	Diagnostic Roentgenology
145.	Sackett, George L.	Cleveland, O.	Radiology
146.	Scott, Harry A.	Lincoln, Neb.	Diagnostic Roentgenology
147.	Senturia, Hyman R.	Chicago, Ill.	Radiology
148.	Sherman, Cyril F.	Wichita, Kans.	Roentgenology
149.	Sickel, Emanuel M.	Lakewood, N. J.	Diagnostic Roentgenology
150.	Silverstone, Sidney M.	New York, N. Y.	Therapeutic Radiology
151.	Singer, Bella	Elizabeth, N. J.	Diagnostic Roentgenology
152.	Sirca, Dionisie M.	Springfield, Ill.	Roentgenology
153.	Sisk, J. Newton	Madison, Wis.	Radiology
154.	Smith, Barney B.	Buffalo, N. Y.	Roentgenology
155.	Smith, Earl D.	Utica, N. Y.	Radiology
156.	Smith, Ernest E.	New York, N. Y.	Radiology
157.	Sokow, Theodore	Kenosha, Wis.	Radiology
158.	Solomon, Bennet	Springfield, Mass.	Diagnostic Roentgenology
159.	Southworth, J. D.	Rutland, Vt.	Therapeutic Radiology
160.	Spencer, Earle W.	Saskatoon, Sask.	Radiology
161.	Stacy, Archie J.	Tupelo, Miss.	Diagnostic Roentgenology
162.	Sternbergh, W. C. A.	Clifton Springs, N. Y.	Radiology
163.	Stewart, Calvin B.	Atlanta, Ga.	Therapeutic Radiology
164.	Szymanski, John J.	Passaic, N. J.	Radiology
165.	Talley, Louis F.	Marshalltown, Ia.	Roentgenology
166.	Thompson, William G.	Holden, Mo.	Radiology
167.	Truog, Clarence P.	Minneapolis, Minn.	Roentgenology
168.	Tyner, Furman H.	Port Arthur, Tex.	Radiology
169.	Vaughn, Robert J.	Annapolis, Md.	Roentgenology
170.	Wallace, William S.	Durham, N. C.	Radiology
171.	Ward, Leo J.	Elizabeth, N. J.	Diagnostic Roentgenology
172.	Warden, Ralph H.	Chicago, Ill.	Roentgenology
173.	Webb, Harold H.	Ottumwa, Ia.	Radiology
174.	Wehr, William H.	Buffalo, N. Y.	Therapeutic Radiology
175.	Weinstein, Samuel	Brooklyn, N. Y.	Roentgenology
176.	Weitz, Harry L.	Traverse City, Mich.	Roentgenology
177.	Williams, Edwin G. C.	Danville, Ill.	Therapeutic Radiology
178.	Willis, Augusta Elizabeth	Orangeburg, S. C.	Roentgenology
179.	Wilson, Angus K.	Norfolk, Va.	Radiology
180.	Wilson, Russell F.	Beloit, Wis.	Radiology
181.	Worth, Harry M.	Victoria, B. C.	Radiology
182.	Wright, Hobart H.	Ann Arbor, Mich.	Radiology
183.	Zielinski, John B.	Fall River, Mass.	Radiology

A NOTE OF CORRECTION

Word has been received from James F. Brailsford, M.D., of Birmingham, England, that the word "chondroma" (Radiology, **33,** 494, October, 1939), fourth line from bottom of page, first column, and in the caption to Figure 10 on the same page, should read "chordoma."

IN MEMORIAM

Word has been received of the death of four members of the Radiological Society of North America: Milo Wilson, M.D., of Gallipolis, Ohio; Prof. F. K. Richtmyer (associate), of Ithaca, N. Y.; Morgan D. Baker, M.D., of San Jose, Calif., and Bernhard Friedlaender, M.D., of Detroit, Michigan. The friends and associates of these late members will grieve to learn of their passing.

BOOK REVIEW

DIFFERENTIALDIAGNOSTIK DER LUNGENERKRANKUNGEN IM RÖNTGENBILDE (Roentgenographic Differential Diagnosis of Diseases of the Lungs), with Special Consideration of the Lateral Position. By Dr. O. SIMON, head of the Roentgenologic Division of the Medical Clinic, University of Koenigsberg. A volume of 84 pages, with 204 illustrations. Published by Georg Thieme, Leipzig, 1939. Price: 19.00 R.M. (25 per cent discount allowed to foreign purchasers).

This small volume, another one of the series of supplements to the *Fortschritte auf dem Gebiete der Röntgenstrahlen*, is essentially an atlas, the major portion being occupied by excellent positive reproductions of postero-anterior and lateral roentgenograms of the chest. In the foreword by Professor Assmann, great stress is laid upon the need for films of the chest to be made in two positions, at right-angles to each other. Accordingly, the lateral views are emphasized.

The cases are grouped in unique fashion, various pathologic entities which produce similar roentgenologic findings being treated in each section. The discussion is divided into the following groups: extra-pulmonary involvement including chest wall processes and pleural lesions; small sized pulmonary lesions, including miliary processes, vascular changes, etc., involvement of gross pulmonary segments, such as atelectasis, pneumonia, tuberculosis, etc., cavitations and enlargements of lymph nodes; changes in the diaphragms, and finally, bronchial tumors. The illustrations are well selected and instructively grouped. This is an excellent volume for the study of the differential diagnosis of pulmonary and pleural diseases.

ABSTRACTS OF CURRENT LITERATURE

CONTENTS BY SUBJECT

THE FOLLOWING ABSTRACTORS HAVE CONTRIBUTED TO THIS ISSUE

JAMES J. CLARK, M.D., of Atlanta, Ga.
JOSEPH T. DANZER, M.D., of Oil City, Penna.
SYDNEY J. HAWLEY, M.D., of Danville, Penna.
HANS W. HEFKE, M.D., Milwaukee, Wisc.
JOHN B. MCANENY, M.D., of Madison, Wisc.
ANTONIO MAYORAL, M.D., of New Orleans, La.
JOHN M. MILES, M.D., of Lafayette, La.
LESTER W. PAUL, M.D., of Madison, Wisc.
HAROLD O. PETERSON, M.D., of Minneapolis, Minn.
ERNST A. POHLE, M.D., Ph.D., of Madison, Wisc.
ERNST A. SCHMIDT, M.D., of Denver, Colo.
CHARLES G. SUTHERLAND, M.D., of Rochester, Minn.
WILLIS A. WARD, M.D., of Chicago, Ill.

ABSTRACTS IN THIS ISSUE LISTED ALPHABETICALLY BY AUTHORS

ANEURYSM

Cardiac Aneurysm. John Parkinson, D. Evan Bedford, and W. A. R. Thomson. British Jour. Radiol., **12,** 129–149, March, 1939.

This paper deals with left ventricular aneurysm, a condition which was formerly thought to be very rare. The latest reliable figures show that cardiac aneurysm is found in 9 per cent of cases of cardiac infarction examined at necropsy. The authors have accumulated autopsy records of 16 cases. The varieties shown are arteriosclerotic, syphilitic, mycotic, rheumatic, congenital, and traumatic. The commonest cause is coronary occlusion, found in 13 of the 16 cases. Eleven were of the left anterior descending branch. Usually the aneurysm is a sac or bulge, varying in size from that of a small nut to the size of an aortic aneurysm, located on the anterior wall in or near the apex. In some cases it is saccular. It is relatively rare on the posterior wall. The wall of the aneurysm is usually thin and composed of fibrous tissue. The pericardium is always adherent. The interior usually contains a clot which occasionally shows calcification. Rupture is rare. Aneurysms are much more common in males. The average age is 56 years.

The clinical signs are: increased area of the cardiac dullness, increased precordial pulsation often not coinciding with the apex, and pericardial friction. There is usually a history of coronary occlusion. Anginal pain occurs occasionally. The blood pressure is not raised. Paroxysmal tachycardia occurs. Electrocardiographic tracings usually show the characteristics of infarction of the anterior wall of the left ventricle.

The average duration of life was 23 months from the attack of coronary thrombosis and ten months from the time of diagnosis. Only seven of the 15 cases reported herein had died. Four died of congestive heart failure, two died suddenly, and one of cerebral embolism. Some patients do surprisingly well considering their disease.

The roentgenographic findings are enlargement of the left ventricle with deformity of its contour, localized protuberance inseparable from the heart shadow, abnormal or absent pulsation in the aneurysmal zone, evidence of adhesions between the heart, the chest wall, and diaphragm, calcification in the wall or the clot. The deformities are usually visible in the anterior and oblique views. The correct obliquity can sometimes be determined only by fluoroscopy. Expansile pulsation is often absent. Some aneurysms are concealed by the diaphragm.

If the aneurysm is in the anterior wall of the left ventricle, the heart is usually enlarged to the left and its contour deformed. If it is in the lower half, the apex will be blunted. It may, if it is in the upper half, produce a diffuse bulge upward or a localized protrusion. In the right oblique view such an aneurysm projects forward, producing a distinct ledge. Aneurysms of the posterior wall are rare and are best seen in the left oblique view with the esophagus filled with barium. Aneurysms of the interventricular septum are apt to produce a marked enlargement to the right.

Calcification in the clot or the wall must be differentiated from other calcifications. Those in the aneurysm are linear and even, and within the heart contour.

Differential diagnosis must be made between aneurysm and enlarged left ventricle from high blood pressure, enlarged conus arteriosus, aneurysms of the descending aorta, and non-cardiac vascular tumors in the chest.

Case reports of 15 cases are given.

SYDNEY J. HAWLEY, M.D.

Intrathoracic Aneurysms. Peter Kerley. British Jour. Radiol., **12,** 158–162, March, 1939.

These observations are based on 62 cases. The symptoms in the majority were misleading, 60 per cent being predominantly pulmonary. Pressure on the trachea and bronchi causes bronchitis and dyspnea. Hemoptysis is usually secondary to the bronchitis or pressure on a large vein. The Wassermann test was negative in three cases and doubtful in one. A negative Wassermann test does not exclude aneurysm.

Aneurysms are slightly more frequent on the ascending portion. The important roentgen signs are constant relation between the tumor and the aorta, linear and sickle-shaped areas of calcification, pressure effects on neighboring structures, expansile pulsation, the globular shape of the tumor, and cardiac enlargement. Expansile pulsation is present in only about 25 per cent of the cases. The tumors may be irregular in shape because of daughter aneurysms and adhesions causing distortion. Kymographic examinations will permit correct diagnosis in 98 per cent of the cases. Mistakes occur in dissecting aneurysms and in cases in which the aneurysm is concealed by a collapsed lung.

SYDNEY J. HAWLEY, M.D.

ANIMAL EXPERIMENTATION

The Production of Transplantable Carcinoma and Sarcoma in Guinea Pigs by Injections of Thorotrast. L. Foulds. Am. Jour. Cancer, **35,** 363–373, March, 1939.

There are few records of the experimental production of tumors in guinea pigs. Neither tar nor a carcinogenic hydrocarbon has produced cancer of the skin. Foulds made four injections of 0.2–0.3 c.c. of thorotrast into the base of a nipple and produced tumors in four out of nine guinea pigs, which survived until the earliest growth was detected. Average induction time was 37 months. The tumors comprised one carcinoma, two sarcomas, and a fibrosarcoma. The first three were transplantable.

HAROLD O. PETERSON, M.D.

Osteochondritis Deformans Juvenilis in Dogs. P. C. Eichholtz and A. M. Ernst. Tijdschrift voor Diergeneeskunde, **66,** 179–183, February, 1939.

According to the authors, this is the first time that typical Perthes' disease has been described in dogs. The roentgenographic details completely corresponded with those observed in the human (flattening and decalcification of the head of the femur, shortening of the

femoral neck, etc.). The disease was diagnosed in six young dogs which had never been ill before. Clinically, the disease manifested itself in lameness and limping of one hind leg. These symptoms were first slight and seemed to disappear after one or two days but later reappeared and were then much more pronounced. Abduction and rotation of the hip joint were limited; the pain reaction varied considerably.

The observation and history of the dogs failed to throw any light on the etiology or intrinsic character of Perthes' disease.

ERNST A. SCHMIDT, M.D.

The Influence of Wave Length on the Biological Effectiveness of Radiation. Herbert G. Crabtree and L. H. Gray. British Jour. Radiol., **12,** 39–53, January, 1939.

Reported results of the influence of wave length on the biological effect of radiation are conflicting. Some of these discrepancies are probably due to differences in the physical condition of the tissue at the time of radiation, difference in the absorbing ability of different tissues used, and inaccuracies in physical and biological measurements. It has been shown that the type of metabolic change is dependent upon the temperature of the tissues during radiation.

In these experiments, the effect of radiation was estimated by its ability to inhibit anærobic glycolysis in isolated retinas of rats. This tissue is suitable as its metabolism closely resembles that of tumor tissue. Small doses of radiation quickly alter the metabolic process. Anærobic glycolysis is readily inhibited by radiation and it is readily measured. The question of mitosis does not come up, as the tissue consists of nondividing cells. Since it has been shown that there is no significant difference between the metabolism of the retinas from the two eyes of the same rat, one was used for the experiment and the other for a control.

The conditions of the experiments are described in detail, including the preparation of the tissue, measurement of anærobic glycolysis, and measurement of the radiation. Comprehensive tables and graphs showing the results are given.

The results are remarkably consistent, even when the inevitable slight variations of dose and inherent difference in sensitivity of the retinas of various rats are considered. There is nothing to indicate whether or not there is any correlation between the magnitude of anærobic glycolysis and radiosensitivity. Retinal glycolysis is excessively sensitive to radiation. The maximum inhibition obtained with 10,000 r was about 70 per cent. The slope of the curves indicates that very much higher doses would be necessary to increase this materially. From these experiments and others previously reported, it would appear as though there were two types of glycolysis—a highly vulnerable fraction which represents about 65 per cent of the total, and a more resistant fraction which makes up the remainder. If this is so, it is evidence of a selective action of radiation.

The general conclusion from these experiments is that the amount of reduction of anærobic glycolysis in isolated retinas of rats is the same for equal intensities of beta, gamma, and x-radiation.

S J. HAWLEY, M.D.

APPARATUS

The Absolute Determination of the r Unit in the Radiological Department of the University of Tokio. S. Nishikawa, M. Nakaidzumi, and N. Motida. Strahlentherapie, **64,** 477, 1939.

The authors describe in detail standardization apparatus constructed for the absolute determination of the r unit. They use a large ionization chamber with two parallel aluminum electrodes. The ionization currents are measured according to the *Nul* method of Townsend. Comparisons of the measurements with those carried out by means of the Kuestner instrument showed agreement within 0.07 per cent.

ERNST A. POHLE, M.D., Ph.D.

A Simple Device for Changing the Light Intensity in the X-ray Illuminator. Edward J. Van Liere and David W. Northrup. Jour. Lab. and Clin. Med., **24,** 869, 870, May, 1939.

According to the authors, the ordinary x-ray illuminator or view box used in tracing teleoroentgenograms may generate sufficient heat to injure the film or the film may become so warm that the hand being used for tracing cannot be allowed to rest on it. Also, the intensity of light is difficult, if not impossible, to regulate.

Both these difficulties, they state, can be obviated by the simple insertion, in series with the electric light bulb in the x-ray illuminator, of a foot rheostat such as is used in operating an electric sewing machine. In this manner the warmth of the film and the intensity of light can be regulated by the foot without any disturbance to the tracing hand, and the electric light goes out automatically when the foot is released, so that the light cannot be accidentally left on, thereby ruining the film.

The ability to change the light intensity is an aid in tracing the apex and is also useful in studying some of the ordinary x-ray films. The authors referred, of course, to the view boxes without the mercury vapor lamps.

WILLIS A. WARD, M.D.

Applications of the Stereoradiographic Centering Apparatus in Otology and General Surgery. Part I.—Radiographic Analysis in Otology. Part II.—Combined Method for the Localization and Extraction of Radiopaque Objects by Means of the "Light Compasses." C. Chaussé. British Jour. Radiol., **12,** 76–90, February, 1939.

PART I

Antidiffusion-stereoradiographic Analysis.—This is a method of studying an organ by a series of small examinations of separate parts of the organ. The examinations are made by a special centering stereographic ap-

paratus which the author describes. In examining the mastoid, an exposure 8 cm. in diameter is made. This film is used as a guide, with the patient's head well immobilized, and smaller diametered exposures are made of various parts of the mastoid. The use of the small fields gives a sharp image. Breaking the examination down into small units enables the examiner to equalize better the difference in density of the various parts. By the use of varying incidences of the rays in different parts of the mastoid, more accurate interpretation is possible. The method is useful also in exploring various parts of the cranium.

Tomography.—The author uses repeated exposures on the same film, moving the tube and film as in tomography, but during the exposure the tube and film are motionless. The linear images produced by the parts not in focus are represented by a series of small dots. As they are clearer than the blurred images in ordinary tomography of the structures not in the focal plane, some information about them can be obtained. The stereographic centering apparatus described may be used for this purpose. It will also indicate the level of the focal plane. The technic for using the apparatus in this manner is described.

PART II

By adding lights to the stereoradiographic apparatus, a device is obtained which readily localizes opaque foreign bodies in the body and which can be used to guide the surgeon in finding them. The technic for operating the device is given in detail.

SYDNEY J. HAWLEY, M.D.

BIOLOGIC EFFECTS

Functional Factors in Radiation Therapy. M. Bertolotti. Strahlentherapie, **65,** 87, 1939.

The author analyzes a number of problems touching the relationship between physically absorbed dose and biologic effect. He contends that in addition to the purely physical explanation that the biologic effect of radiation on tissues is a direct function of the absorbed radiant energy, a physiologic factor must be considered which takes into account the properties of the irradiated tissues as well as the place of absorption. The rôle of the sympathetic nervous system in this connection is also discussed.

ERNST A. POHLE, M.D., Ph.D.

Experimental Studies and Theoretical Deductions Regarding the Hypothesis of the Biologic Effect of Roentgen and Gamma Rays on Living Matter. G. G. Palmieri and A. Valenti. Strahlentherapie, **65,** 15, 1939.

The authors studied the relationship between the absorption of radiant energy and the biologic reaction, using the skin erythema as test. If the two processes were running parallel, then the effect in the skin should decrease with increasing frequency of the radiation. However, it was found that for 2 kv. a surface dose of 6,000 r corresponded to the erythema dose while the corresponding figures for 150 and 500 kv. were 450 and 1,200 r, respectively. Consequently, the authors deduced that the effect on the skin is not proportional to the energy absorbed as measured by ionization. The possibility of a non-specific action or a catalytic effect in explanation of these observations is discussed.

ERNST A. POHLE, M.D., Ph.D.

BIOLOGIC EXPERIMENTATION

Further Studies with Seedlings on the Question of Wave Length Dependence of Radiobiological Reactions. P. S. Henshaw and D. S. Francis. Am. Jour. Cancer, **35,** 386–400, March, 1939.

Triticum and *Lycopersicum* seedlings were treated with 200 and 700 kv. x-rays. In some experiments the seedlings were surrounded with a low atomic weight material. *Lycopersicum* seedlings were more sensitive to 700 kv. radiation in all the experiments. They were more sensitive by 42 per cent when the low atomic material was used and by 122 per cent when it was not. These findings are taken as evidence that there is a differential response on the part of the organism to different qualities of radiation.

HAROLD O. PETERSON, M.D.

Some Unsolved Problems of Radiation Biology. P. del Buono. Strahlentherapie, **65,** 108, 1939.

The author undertook a series of experiments in order to study the effect of the wave length on the biologic effect. He exposed the seeds of peas, wheat, and millet to x-rays (from 140 to 180 kv., doses from 25 to 1,000 r, one, three, and six days after germination had begun). The length of the seedlings was carefully recorded and the results plotted in graphs. It appeared that for the type of radiation used and for any type of radiation there exists the possibility of stimulation. After any irradiation, even after a dose of 25 r, an injury even if slight must be expected. For doses of 100 r and above, the degree of injury increases with the dose. For plants there is a certain period during the growth when the radiosensitivity is at a maximum. It cannot be determined yet whether this is specific for the individual type of plant or whether it is due to a general biophysical factor. The phenomena observed were independent of the penetration of radiation and of the duration of the exposure. Consequently it is assumed that the biologic effect of radiation depends on the dose and the state of the organism at the time of irradiation.

ERNST A. POHLE, M.D., Ph.D.

BONE DISEASES (DIAGNOSIS)

Hereditary Deforming Chondrodysplasia: Report of Ten Cases in One Family. Charles M. Graney. Jour. Am. Med. Assn., **112,** 2026–2030, May 20, 1939.

This condition was first described in 1825, and so concisely that the description embraces all that is of import regarding it. It has been perhaps best defined as "an hereditary disturbance of bone growth beginning early in childhood and characterized by multiple carti-

laginous and osteocartilaginous growths within or on the skeletal system." Malignant degeneration is said to occur in 5 per cent of cases, but the incidence is probably less than that. In diagnosis, the hereditary factor, the symmetrical distribution of the exostoses, their multiplicity, and the x-ray appearances are important. X-ray examination shows multiple exostoses of the long bones occurring in the epiphyseal region but springing from the diaphysial side and directed away from the epiphyses along the line of muscular pull. The exostoses vary from simple spikes to pedunculated and cauliflower types and from well ossified spurs to typical chondromas. The epiphyses may be misshapen or absent, although they do not produce any exostoses themselves. The bones most frequently affected occur in this order: ulna, fibula, femur, humerus, and phalanges. The carpus, tarsus, vertebræ, skull, and sternum are not involved, since pure cartilaginous or membranous bone escapes this process.

Ehrenfried, in 1915 and 1917, found that the reported cases in the literature totalled about 700.

The etiology of this condition is obscure. The neoplastic theory is not tenable, as growth and development of exostoses stop at the age of from 20 to 22 years with the attainment of skeletal maturity. It is apparently unrelated to rickets or vitamin deficiency; if it were so related, there should be no hereditary factor. The distribution of the disease is the same as that of a thyroid deficiency, and the possibility of a glandular disturbance, as of thyroid or pituitary, has been considered. A failure of the process of breaking down of bone and shaping or modeling of the bone, as described by John Hunter, has been suggested as the cause. Another theory is that it is produced by impressions made on the germ plasm, consequent to fractured bones and their complex healing processes or that the patients "are made susceptible through transmission from past generations of various obnoxious environmental experiences."

These conditions should remain untreated until after bony growth has stopped. Indications for removal are deformity, interference with the function of joints, muscles, or tendons, and evidence of a malignant condition or an increase in size after bony growth has stopped.

CHARLES G. SUTHERLAND, M.D.

The Endocrine Implication of Juvenile Chondro-epiphysitis. Robert L. Schaefer, Fred L. Strickroot, and Frank H. Purcell. Jour. Am. Med. Assn., **112**, 1917–1919, May 13, 1939.

Juvenile chondro-epiphysitis is described as an alteration in shape of the developing epiphyses associated with an apparent aseptic necrosis. Pathologically there may be rarefaction or even cyst-like formation and degeneration. Clinically there is possibility of eventual deformity. Roentgenographically it is characterized by the following changes in the developing osseous centers: diminution in size, decrease in density, rarefaction, fragmentation, irregularity of the ossification contour, and, in general, a fuzzy, ragged appearance of the chondro-epiphyseal structures. Depending on the various structures showing such x-ray changes, almost innumerable proper or descriptive names have been employed. This conglomeration of proper names is confusing in conditions which, we think, are identical and have the same etiology.

The significance of this publication is an attempt to prove that juvenile chondro-epiphysitis is due to an endocrine imbalance, specifically to a primary or secondary hypothyroidism in which the tissue-differentiating factor is absent, that it is a generalized process involving one or more of the developing chondro-epiphyseal structures, and that it is, at least, incipiently asymtomatic.

The roentgenographic study of osseous development ranks to-day as one of our most useful diagnostic procedures. In the age group from birth to eight years it by far outranks the basal metabolic rate for accuracy. In the older age group, from juvenility to completion of adolescence, delayed union or advanced union of the epiphyses gives visual evidence in the x-ray of premature adolescence or sex maturity or of gonadal hypofunction.

In 1931, the authors began to do routine x-ray examinations of all children with suspected endocrinopathies. Very early in their studies of endocrine dwarfism they were struck by the frequency of single or multiple involvement of the chondro-epiphyseal structures. It soon became apparent that this condition was not peculiar to dwarfism but was being seen with as great or greater frequency in other endocrine conditions displaying signs of hypothyroidism. Of 258 endocrinopathic patients studied, 91 (35.2 per cent) showed a chondro-epiphyseal disturbance. The number of hypothyroid cases showing chondro-epiphyseal disturbance was 85 (39.0 per cent). All but six cases were associated with hypothyroidism. Thirty-eight (41.7 per cent) of the 91 showing involvement had multiple epiphyseal lesions. The trochlea of the humerus was most frequently involved. There were only three patients in the entire group who had any symptoms referable to the osseous involvement. In a control group of 99 children with serial roentgenographic examinations at yearly intervals (totalling 2,200 films), only seven (7 per cent) showed evidence of chondro-epiphysitis.

The writers feel that x-ray evidence of this lesion is a definite indication for thyroid therapy.

CHARLES G. SUTHERLAND, M.D.

Punctate Epiphyseal Dysplasia Occurring in Two Members of the Same Family. D. G. Maitland. British Jour. Radiol., **12**, 91–93, February 1939.

A case is reported of a female child, aged three days. The limbs were spastic, and the knee and elbow joints enlarged. Radiographic examination showed punctate areas of calcification in the spine, sacrum, and pelvis. The femora and humeri were shorter and thicker than normal; the proximal ends of the diaphyses were

widened, cupped, and irregular and showed punctate calcification. The mother was normal; the father had developmental defects of the fingers. One sister of the child reported had the same defects; two other siblings were normal.

SYDNEY J. HAWLEY, M.D.

BONE TUMORS

Metastatic Bone Carcinomatosis Associated with Parathyroid Hyperplasia and with Symptoms of Hyperparathyroidism: With Blood Calcium and Phosphorus Studies before and after Extirpation of a Hyperplastic Parathyroid Gland. S. Ben-Asher. Jour. Lab. and Clin. Med., **24,** 709–717, April, 1939.

The author presents a case with metastatic carcinoma associated with parathyroid hyperplasia and with symptoms of hyperparathyroidism, such as hypercalcemia, a negative calcium balance, and increased excretion of calcium in the urine. The gland was removed and the blood calcium became lower, but not to the normal level.

This case and its discussion demonstrate the importance of the roentgenologist's consideration of the possibility of a co-existing hyperparathyroid disease when making a diagnosis of metastatic bone carcinomatosis.

This causes one to consider the hyperplasia of the gland as being secondary to the bone changes.

WILLIS A. WARD, M.D.

Tumors of Bone. Channing C. Simmons. New England Jour. Med., **220,** 629–632, April 13, 1939.

The author adheres to the classification of bone tumors suggested by the Registry of Bone Sarcoma.

Non-malignant osteogenic tumors are usually readily diagnosed but one that contains a preponderance of cartilage should be removed for fear of malignancy.

Osteogenic sarcoma may be osteoblastic or osteolytic, and is described by the prefixes osteo-, chondro-, and myxo-. Metastasis is frequently early and the prognosis poor, no matter what the treatment. The x-ray film always shows bone destruction and bone formation. The periosteum may be elevated by ray formation and the so-called "reactive triangle" may be seen. In diagnosis, the history, film findings, and biopsy should be taken together.

Ewing's sarcoma arises from the shaft of long bones and is characterized by bone destruction with no tumor-bone formation although there may be some reactive new bone. Metastases to lungs and skull occur. Onion-skin appearance of the periosteum is characteristic. It may be confused with osteomyelitis xanthoma and reticulum-cell sarcoma. It is radiosensitive but metastases occur.

Reticulum-cell sarcoma is believed to arise from the reticulo-endothelial system and belongs to the lymphomas. An early x-ray film shows central bone destruction. The tumor is radiosensitive but the best results are believed to follow surgery.

Liposarcoma behaves like an osteogenic sarcoma.

Myeloma is a tumor of the marrow composed of plasma cells, usually multiple but possibly single. X-ray films show multiple areas of destruction. It is usually radioresistant.

The giant-cell tumor arises in the medulla near a joint, causing destruction and expansion of the cortex. The cavity is divided by fine trabeculæ and the tumor is sharply demarcated by a concavo-convex line. The tumor should be irradiated except in cases in which it can be easily removed surgically.

Central angioma of bone is rare and arises near the epiphyseal ends of long bones. It may resemble a giant-cell tumor but the trabeculæ are more marked. Treatment is the same as for the giant-cell tumor.

Metastatic tumors are variable.

Parosteal fibrosarcoma arises from the periosteum, involving bone secondarily and it is less malignant than true osteogenic sarcoma.

J. B. MCANENY, M.D

THE BREAST

The Clinical Significance of a Lump in the Breast. George Crile, Jr. Cleveland Clin. Quart., **6,** 231–240, July, 1939.

Two hundred consecutive cases of breast tumors have been studied and 43 per cent were found to be malignant. Seventy-five per cent of these patients were over 50 years of age. Twenty per cent of the malignancies of the group occurred in the 40- to 50-year group. The only valuable clinical finding is dimpling of the skin, and that is not reliable. The discovery of axillary glands is a late finding. Diagnosis is best established by biopsy.

J. B. MCANENY, M.D.

Irradiation in the Treatment of Cancer of the Breast. U. V. Portmann. Cleveland Clin. Quart., **6,** 109–115, April, 1939.

The greatest event in the treatment of cancer of the breast was the development of a rational surgical technic by Halsted. The percentage of five-year cures reported in the literature varies from 15 to 50 per cent, depending greatly on the choice of cases for operation; the average is about 30 per cent. Any means of increasing the number of cures should certainly be utilized. Classification of carcinoma of the breast based on microscopic examination has virtue but does not tell the whole story, omitting the extent of involvement, for one thing.

Portmann suggests a clinical grouping consisting of: Group I, which includes the freely movable localized tumor without metastasis or skin involvement; Group II, consisting of a freely movable localized tumor without skin involvement but with metastasis to the axillary nodes or other tissues, and Group III, in which there is diffuse involvement of the breast, skin involvement, edema, ulceration or nodules, and metastasis.

With this grouping in mind, 373 cases of breast cancer operated upon by Dr. George Crile were examined.

All cases of Group I lived five years; about 50 per cent of Group II cases lived five years, but in Group III no patient survived the five-year period. None of these patients received irradiation therapy.

Using the same standards of comparison, 235 cases that received post-operative irradiation were examined and it was found that irradiation was of no benefit in Group I cases because they all lived five years without irradiation. Among Group II cases, about 70 per cent survived the five-year period. The cases of Group III showed a five-year survival rate of 10 per cent, but none was without evidence of cancer. In addition, the proportion of patients who survived each yearly period up to five years was higher than the number of those who were operated upon only. What is more this study does not take into account the benefit derived from irradiation in metastasis.

The question of sterilization by pelvic irradiation is not discussed.

An important point presented by this author is a discussion of evidences of incurability, which is difficult to find in the literature. These evidences of incurability are grouped as edema, ulceration, nodules, induration, and inflammation of the skin; edema, diffuse infiltration, multiple tumors, and fixation of the tumor of the breast, and lymph node or distant metastasis.

J. B. McAneny, M.D.

CANCER (THERAPY)

Primary Squamous-cell Carcinoma of the Uvula: Report of Two Cases. J. Milton Robb and Merrill W. Michels. Ann. Otol., Rhinol., and Laryngol., **48,** 521–524, June, 1939.

Primary squamous-cell carcinomas of the uvula are rare. The authors report two cases. Early excision offers a better prognosis than radiation alone, and this was done in the two cases reported. In one, external supervoltage (500 kv.) roentgen therapy was given post-operatively. Both patients have remained well.

Lester W. Paul, M.D.

Metastatic Cancer in the Lymph Nodes of the Neck. Harold G. F. Edwards. Southern Med. Jour., **32,** 905–910, September, 1939.

Radiosensitivity is less in metastatic cancer of the lymph nodes of the neck than in the primary lesion, due, among other reasons, to inflammation, fibrosis, and degenerative changes in the nodes. Frequent examinations for involved nodes are necessary because of the latent period of from eight to ten months before metastasis reveals itself. When the nodes are involved, aspiration biopsy is first done, oral sepsis, if present, is reduced, and treatment instituted at once or a few days after completion of irradiation of the primary lesion.

Small nodes from a primary epidermoid cancer are treated with radium implants sufficient to deliver from seven to ten erythema doses. Small nodes from a transitional or lympho-epithelioma can sometimes be treated with x-rays in fractioned doses, giving 7,000 or 8,000 r over a field not exceeding 4 or 5 cm. Large areas of involvement with invasion of surrounding tissue are treated with external irradiation (200 r daily) for a total up to 3,500 r, followed immediately by transcutaneous implantation of radium needles to bring the total dosage up to from seven to ten erythema doses.

John M. Miles, M.D.

Treatment of Carcinoma of the Vallecula. E. Wessely. Strahlentherapie, **65,** 601, 1939.

Since 1932, the author has treated 21 cases of cancer of the epiglottis and the base of the tongue. Nineteen were men, two were women; the age fluctuated between 50 and 60 years, the youngest being 38 and the oldest 73. Histologically, the tumors were mostly squamous-cell carcinoma; in over half of the cases there were definite glandular metastases. Most of the patients were given x-ray therapy applied according to the method of Coutard; the dose effective in the tumor was 2,500 r and given through two fields. Residual tumor tissue was treated with radium either by means of surface applicators or by interstitial irradiation (5 mg. needles). Five cases remained free from recurrence for over one year; one for two years; three for three years; one for four years; one for seven years, and one for eight years. In conclusion, the author emphasizes the importance of a thorough examination of the base of the tongue and the epiglottis in older persons who complain of vague disturbances when swallowing.

Ernst A. Pohle, M.D., Ph.D.

Radio-surgical Treatment of Carcinoma of the Stomach. A. Salotti. Strahlentherapie, **65,** 121, 1939.

The author relates his experience in the treatment of carcinoma of the stomach by means of interstitial and contact radium therapy. After exposure of the tumor, from 1,176 to 2,400 mg.-hr. are applied interstitially or from 2,000 to 3,000 mg.-hr. if contact screens are used. This requires a treatment time of from 40 to 70 hours. No immediate or late injuries of the neighboring organs have been observed. A series of roentgenograms shows the needles *in situ* and also the roentgenologic appearance of the stomachs of some patients before and after treatment. The advantages of the method are that the stomach remains intact in the body, that it requires only an ordinary incision, and that it is apparently possible to give doses sufficiently high to destroy the tumor without injury to the surrounding normal tissue.

Ernst A. Pohle, M.D., Ph.D.

What can One Expect from Radiation in Carcinoma of the Rectum and Anus? Orville N. Meland. California and West. Med., **50,** 403–407, June, 1939.

The author's discussion and review of the effects of radiation in carcinoma of the rectum and anus are very good. He divides his cases into three groups—inoperable, recurrent, and operable.

In the first group he hoped for nothing but palliation;

in the second group therapy was given to retard the growth, as well as to relieve pain. The patients in these first two groups had only a short period of life.

In the operable group, Meland believes surgery offers the greatest hope of recovery, especially now that the surgical procedures have been standardized. He expects improved radiation results, since radiation treatment is also becoming more standardized. Many cases require both x-radiation and radium.

In a majority of cases, radiation will stop bleeding and pain, and, occasionally, an inoperable case will apparently become operable. This last statement is open to question.

In general, the results of any method of treatment are not satisfactory, as a very high percentage of cases have metastasized before diagnosis has been made. Therefore, any type of treatment is more or less palliative.

JAMES J. CLARK, M.D.

CHOLECYSTOGRAPHY

Some Practical Considerations of Cholecystography from the Roentgenologic Aspect. Eugene P. Pendergrass. Pennsylvania Med. Jour., **42,** 787–790, April, 1939.

The author gives the technic of the double-dose administration of dye and also his roentgen technic which is commonly used by most radiologists.

A suggested nomenclature of the findings in cholecystography is given in detail.

A few of the more common points of differential diagnosis are given, and a number of sources of error are mentioned.

JOSEPH T. DANZER, M.D.

THE COLON

Diffuse Polyposis of the Large Bowel, with a Case Report. A. Y. Mason. South African Med. Jour., **13,** 237–239, April 8, 1939.

The author describes a case of diffuse colonic polyposis in a 33-year-old Greek electrician who complained of colicky abdominal pains, distention, bloody stools, and diarrhea. A conclusive investigation of the family history of the patient was impossible, but there was suspicion that the patient's father suffered and died of the same disease, which is assumed to be of familial character. Mason points out that, in view of the almost inevitable malignant degeneration of the polypi, treatment is a most urgent problem, be it x-ray deep therapy, colectomy, or surgery combined with fulguration. Although theoretically consenting to treatment, Mason's patient had to date put off the suggested operation. Eight months after diagnosis, he was apparently in good general health, and had succeeded in keeping his symptoms in abeyance by diet and regular daily doses of liquid paraffin.

ERNST A. SCHMIDT, M.D.

Roentgen Diagnosis of *Polyposis coli*. A. Knetsch. Röntgenpraxis, **11,** 349–353, June, 1939.

There are two types of polyposis of the colon: one on the basis of an ulcerative or dysenteric colitis; the other the genuine polyposis. In the latter, the inflammatory changes are denied by most authors. It is considered a true neoplastic disease, often hereditary and familial in occurrence. Carcinomatous degeneration is said to take place in from 50 to 60 per cent of these cases (according to Thorbecke and Doering).

A case of extensive polyposis of the colon is described. Two polyps in the rectum had become malignant, as proved by surgery. The combined air-barium enema showed the typical roentgen signs of the disease.

HANS W. HEFKE, M.D.

CONTRAST MEDIA

Should the Use of Thorium Dioxide in Hepatosplenography be Abandoned? Enrico Benassi. Radiol. Med., **26,** 81–98, February, 1939.

Professor Benassi does not agree with the pessimistic view of some observers who condemn this method of exploring the liver and the spleen because it is too dangerous. He believes that the radio-active substances injected into the organism have not been proven by clinical observations to have a deleterious action on the healthy or sick organism, nor on the evolution of disease, and he affirms that the only justifiable objection that exists to-day against the method is possible delayed damage to the tissues brought about by the feeble radio-activity of the thorium remaining for a long time within the body. This is hypothetical, however.

The use of the salt brings a positive visualization of the spleen and liver, a very helpful aid in differentiating subdiaphragmatic tumors. The method has a definite clinical value.

ANTONIO MAYORAL, M.D.